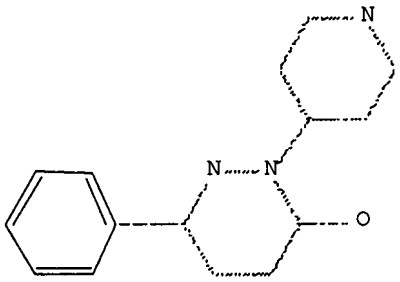
***** INVENTOR RESULTS *****

=> d his l24

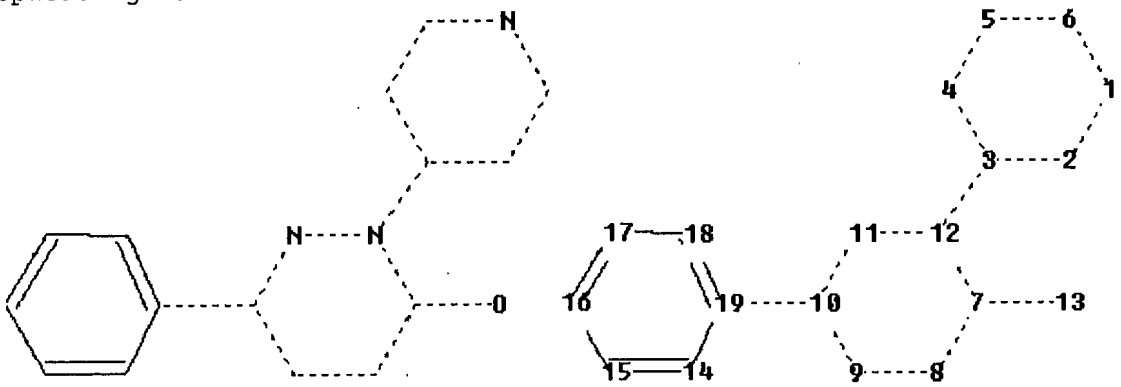
(FILE 'HCAPLUS' ENTERED AT 13:34:15 ON 17 OCT 2007)
L24 13 S L21 OR L23

=> d que l24
L9 STR



Structure attributes must be viewed using STN Express query preparation:

Uploading L3.str



chain nodes :
13
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 14 15 16 17 18 19
chain bonds :
3-12 7-13 10-19
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 14-15 14-19 15-16
16-17 17-18 18-19
exact/norm bonds :
1-2 1-6 2-3 3-4 3-12 4-5 5-6 7-8 7-12 7-13 8-9 9-10 10-11 10-19 11-12

normalized bonds :
14-15 14-19 15-16 16-17 17-18 18-19

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom

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L12          258 SEA FILE=REGISTRY SSS FUL L9
L14           27 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12
L19           79 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENGE W?/AU
L20           88 SEA FILE=HCAPLUS ABB=ON  PLU=ON  STERK G?/AU
L21            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 AND L20
L22          158 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 OR L20
L23           11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L22 AND L14
L24           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 OR L23


=> d his l37

     (FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE, HCAPLUS' ENTERED AT 13:47:09 ON 17
     OCT 2007)
L37           23 S L36 NOT L18
                 SAVE TEMP L37 JAI836MULTIN/A

     FILE 'STNGUIDE' ENTERED AT 13:50:39 ON 17 OCT 2007

=> d que l37
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L9               STR
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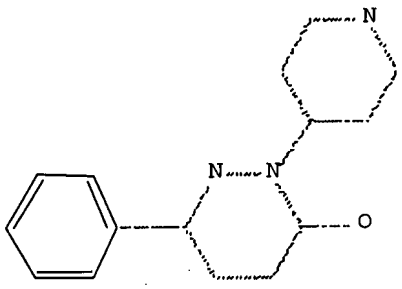

Structure attributes must be viewed using STN Express query preparation:

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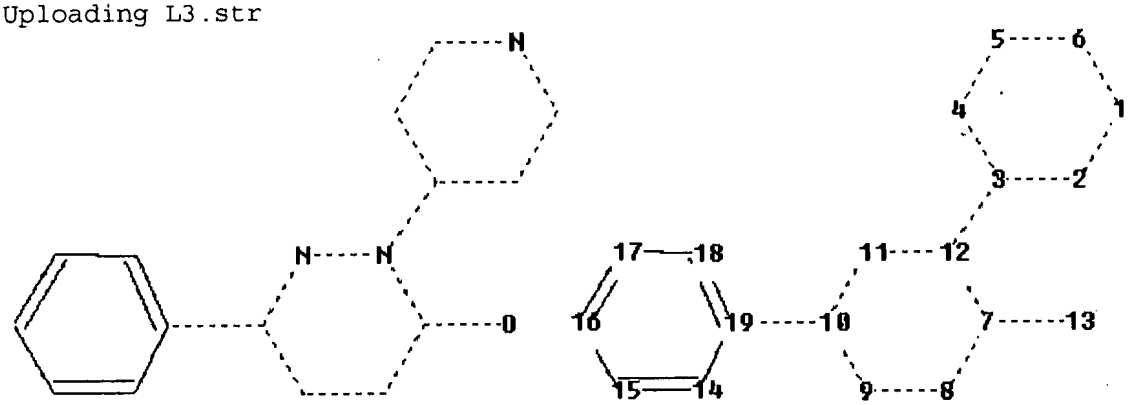

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chain nodes :
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ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  14  15  16  17  18  19
chain bonds :
3-12  7-13  10-19
ring bonds :
1-2  1-6  2-3  3-4  4-5  5-6  7-8  7-12  8-9  9-10  10-11  11-12  14-15  14-19  15-
16
16-17  17-18  18-19
exact/norm bonds :
1-2  1-6  2-3  3-4  3-12  4-5  5-6  7-8  7-12  7-13  8-9  9-10  10-11  10-19  11-12

normalized bonds :
14-15  14-19  15-16  16-17  17-18  18-19


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:CLASS  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom



L12          258 SEA FILE=REGISTRY SSS FUL L9
L14           27 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12
L15           26 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 NOT L5
L16           25 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L15 AND (AY<2005 OR PY<2005
                 OR PRY<2005)
L17              QUE  ABB=ON  PLU=ON  PHARMAC?/SC,SX
L18           18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 AND L17
L19           79 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENGE W?/AU
L20           88 SEA FILE=HCAPLUS ABB=ON  PLU=ON  STERK G?/AU
L22          158 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L19 OR L20
L28          348 SEA L22
L29           26 SEA L28 AND (PDE4(W) INHIBIT? OR PYRIDAZIN?)
L31            9 SEA PHOSPHODIESTERASE(W) 4 AND L28
L32           27 SEA L29 OR L31
L36           26 SEA L32 AND PHTHALAZINONE?
L37           23 SEA L36 NOT L18


=> dup rem l24 l37
FILE 'HCAPLUS' ENTERED AT 13:51:40 ON 17 OCT 2007
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PROCESSING COMPLETED FOR L24
PROCESSING COMPLETED FOR L37
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L38 24 DUP REM L24 L37 (12 DUPLICATES REMOVED)
ANSWERS '1-20' FROM FILE HCAPLUS
ANSWER '21' FROM FILE MEDLINE
ANSWERS '22-24' FROM FILE BIOSIS

=> d l38 1-24 ibib ab

L38 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:284653 HCAPLUS Full-text
DOCUMENT NUMBER: 139:22170
TITLE: Synthesis and Structure-Activity Relationships of cis-Tetrahydrophthalazinone/**Pyridazinone** Hybrids: A Novel Series of Potent Dual PDE3/ **PDE4 Inhibitory** Agents
AUTHOR(S): Van der Mey, Margaretha; Bommele, Kirsten M.; Boss, Hildegard; Hatzelmann, Armin; Van Slingerland, Mike; **Sterk, Geert J.**; Timmerman, Hendrik
CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research, Division of Medicinal Chemistry, Department of Pharmacochemistry, Vrije Universiteit, Amsterdam, 1081 HV, Neth.
SOURCE: Journal of Medicinal Chemistry (2003), 46(10), 2008-2016
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:22170
AB A new series of phthalazinone/pyridazinone hybrids I [R1 = Me, Et; R2 = Cl, MeO, EtO, cyclopentyloxy; X = none, CH2CONH, (CH2)4O, (CH2)4CONH] and II were synthesized and their PDE3 and PDE4 inhibitory activities in vitro and in vivo were investigated. These compds. combine the pharmacophores of recently discovered 4a,5,8,8a-tetrahydro-2H-phthalazin-1-one-type inhibitors of PDE4 and the well-known 2H-pyridazin-3-one-type PDE3 inhibitors such as the tetrahydrobenzimidazoles. All I and II showed potent PDE4 inhibitory activity (pIC50 = 7.0-8.7), whereas the pIC50 values for inhibition of PDE3 vary from 5.4 to 7.5. In general, analogs with a 5-methyl-4,5-dihydropyridazinone moiety exhibit the highest PDE3 inhibitory activities. The highest in vivo antiinflammatory activity is displayed by phthalazinones II [R1 = Et, R2 = EtO; R1 = Me, R2 = Cl; X = (CH2)4O] showing, at a dose of 30 μmol/kg po, 46% inhibition of arachidonic acid (AA) induced mouse ear edema. No correlation was found between the in vitro PDE3 and/or PDE4 inhibitory activity and the in vivo antiinflammatory capacity after oral dosing.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2002:145040 HCAPLUS Full-text
DOCUMENT NUMBER: 136:340646
TITLE: Novel Selective Phosphodiesterase (**PDE4**) **Inhibitors**. 4. Resolution, Absolute Configuration, and **PDE4 Inhibitory** Activity of cis-Tetra- and cis-Hexahydrophthalazinones
AUTHOR(S): Van der Mey, Margaretha; Boss, Hildegard; Couwenberg, Dennis; Hatzelmann, Armin; **Sterk, Geert J.**; Goubitz, Kees; Schenk, Henk; Timmerman, Hendrik
CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research Division of Medicinal Chemistry Department of Pharmacochemistry, Vrije Universiteit, Amsterdam, 1081 HV, Neth.
SOURCE: Journal of Medicinal Chemistry (2002), 45(12), 2526-2533

CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:340646

AB Recently, we reported that 4-catechol-substituted cis-(±)-4a,5,6,7,8,8a- hexa- and cis-(±)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-ones show potent inhibition of phosphodiesterase (PDE4) activity, while the corresponding trans racemic mixts. exhibit only weak to moderate activity. To determine the absolute configuration and PDE4 inhibitory activity of the individual cis-enantiomers, several optically active phthalazinones have been synthesized. The enantiomers of the various γ-keto acids, used as starting materials, were resolved in a classical way by the formation of diastereomeric salts, and each was converted to optically active phthalazinone in an enantioselective manner. The absolute configuration of the (+)-enantiomer of cis-hexahydrophthalazinone (+)-I was determined by X-ray crystallog. The carbon atoms at the 4a and 8a positions were found to have the S- and R-configuration, resp. In the present series of hexa- and tetrahydrophthalazinones, stereoselectivity for PDE4 inhibition is observed; the cis-(+)-enantiomers of the phthalazinones display high inhibitory activity, whereas their (-)-counterparts exhibit only weak to moderate activity. It is likely that all cis-(+)-phthalazinones have a (4aS,8aR)-configuration and vice versa for the cis-(-)-analogs. In the current series, the N-adamantan-2-yl analog (+)-II (R = Me, R1 = 2-adamantyl) shows the most potent inhibition of PDE4 (pIC50 = 9.3); the corresponding (-)-enantiomer is 250-fold less active. In addition, the N-substituted tetrahydrophthalazinones under study were investigated for their in vivo antiinflammatory activities by examining the suppression of arachidonic acid (AA) induced mouse ear edema formation. In this assay analogs (+)-II (R = Me, R1 = 2-adamantyl) and (+)-II (R = Et, R1 = 4-carboxyphenyl) were found to be potent antiinflammatory agents showing about 50% inhibition at 30 μmol/kg po.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:357897 HCAPLUS Full-text
DOCUMENT NUMBER: 137:63213
TITLE: Novel Selective **PDE4 Inhibitors.** 3. In Vivo Antiinflammatory Activity of a New Series of N-Substituted cis-Tetra- and cis-Hexahydrophthalazinones
AUTHOR(S): Van der Mey, Margaretha; Boss, Hildegard; Hatzelmann, Armin; Van der Laan, Ivonne J.; **Sterk, Geert J.**; Timmerman, Hendrik
CORPORATE SOURCE: Division of Medicinal Chemistry, Department of Pharmacochemistry, Leiden/Amsterdam Center for Drug Research, Vrije Universiteit, Amsterdam, 1081 HV, Neth.
SOURCE: Journal of Medicinal Chemistry (2002), 45(12), 2520-2525
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:63213

AB The synthesis and biol. activities of a series of N-substituted cis-4a,5,6,7,8,8a-hexa- and cis-4a,5,8,8a-tetrahydro-2H-phthalazin-1-ones I [XY = (CH2)2, HC:CH; R = Me, cyclopentyl, allyl, PhCOCH2, etc.] are described. It was found that compds. bearing a cycloalkyl group at the 2-position exhibit the highest PDE4 inhibitory activities (pIC50 = 8.6-9.4). The N-cycloheptyl- and N-adamantanyltetrahydrophthalazinones I (XY = HC:CH; R = cycloheptyl, 2-

adamantyl) and II [R1 = R2 = Me, R1R2 = (CH2)4] show high in vivo antiinflammatory activities after oral application. Addnl., some phthalazinones were found to exhibit potent suppression of LPS-induced TNFα release and show moderate potency against fMLP-stimulated production of ROS.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:823689 HCAPLUS Full-text
DOCUMENT NUMBER: 143:229869
TITLE: Preparation of phthalazinone derivatives as PDE4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christiaans, Johannes A. M.; **Menge, Wiro M. P. B.; Sterk, Geert Jan**
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075457	A1	20050818	WO 2005-EP50417	20050201
WO 2005075457	A8	20060302		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1720854	A1	20061115	EP 2005-701632	20050201
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: EP 2004-2423 A 20040204
WO 2005-EP50417 W 20050201

OTHER SOURCE(S): CASREACT 143:229869; MARPAT 143:229869

AB Title compds. I [R1 and R2 are both H or together from an addnl. bond; R3 = (un)substituted phenyl; R4 = OH, alkoxy, NHR5, etc.; R5 = OH, alkoxy or alkoxyalkyl; n = 0, 2, 3, or 4] and their pharmaceutically acceptable salts, are prepared and disclosed as PDE4 inhibitors. Thus, e.g., II was prepared by coupling of (4aS,8aR)-4-(3,4-dimethoxy-phenyl)-2-piperidin-4-yl- 4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (preparation given) with succinic anhydride. The inhibitory activity of I was evaluated using two different methods utilizing cAMP and it was revealed that compds. of the invention displayed -logIC50 values in the range of 8.4 up to 10.4 mol/L. I as inhibitor of PDE4 should prove useful in the treatment of airway disorders. Pharmaceutical compns. comprising I are disclosed.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:823688 HCAPLUS Full-text

DOCUMENT NUMBER: 143:229868
TITLE: Preparation of piperidinyl pyridazinone derivatives as PDE4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christiaans, Johannes A. M.; **Menge, Wiro M. P. B.; Sterk, Geert Jan**
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075456	A1	20050818	WO 2005-EP50415	20050201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005210042	A1	20050818	AU 2005-210042	20050201
CA 2554797	A1	20050818	CA 2005-2554797	20050201
EP 1716133	A1	20061102	EP 2005-716609	20050201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				
JP 2007520528	T	20070726	JP 2006-551846	20050201
US 2007179146	A1	20070802	US 2006-587836	20060816
PRIORITY APPLN. INFO.:			EP 2004-2420 A	20040204
			WO 2005-EP50415 W	20050201

OTHER SOURCE(S): MARPAT 143:229868

AB Title compds. I [R1 and R2 independently = alkyl; R3 = (un)substituted phenyl; R4 = COR5, S(O)2R6(CH2)nCOR7 or CO(CH2)mR8; R5 = alkyl, NR9R10 or (un)substituted phenyl; R6 = alkyl, NR11R12 or (un)substituted phenyl; R7 = NR13R14; R8 = NR15R16; R9-16 independently = H, alkyl, cycloalkyl, etc.; n = 1-4; m = 1-4] and their pharmaceutically acceptable salts, are prepared and disclosed as PDE4 inhibitors. Thus, e.g., II was prepared by coupling of 6-(3,4-dimethoxyphenyl)-4,4-dimethyl-2-piperidin-4-yl-4,5-dihydro-2H- pyridazin-3-one (preparation given) with 2-cyanobenzenesulfonyl chloride. The inhibitory activity of I was evaluated using scintillation proximity assay and it was revealed that selected compds. of the invention displayed -logIC50 values in the range of 7.60 up to 9.68 mol/L. I as inhibitor of PDE4 should prove useful in the treatment of airway disorders. Pharmaceutical compns. comprising I are disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:823673 HCAPLUS Full-text
DOCUMENT NUMBER: 143:229867
TITLE: Preparation of pyridazinone derivatives as PDE4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard;

Kley, Hans-Peter; Christiaans, Johannes A. M.; **Menge, Wiro M. P. B.; Sterk, Geert Jan**
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075437	A1	20050818	WO 2005-EP50412	20050201
WO 2005075437	A8	20060302		
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EP 1716123	A1	20061102	EP 2005-707902	20050201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, IS				

PRIORITY APPLN. INFO.: EP 2004-2413 A 20040204
WO 2005-EP50412 W 20050201

OTHER SOURCE(S): MARPAT 143:229867

AB Title compds. I [R1 and R2 independently = alkyl; R3 = (un)substituted phenyl; R4 = OH, halo, CN, etc.] and their pharmaceutically acceptable salts, are prepared and disclosed as PDE4 inhibitors. Thus, e.g., II was prepared by cyclization of 4-(3,4-dimethoxyphenyl)-2,2-dimethyl-4-oxo- butyric acid (preparation given) with 4-hydrazinobenzoic acid. The inhibitory activity of I was evaluated using scintillation proximity assay and it was revealed that selected compds. of the invention displayed -logIC50 values in the range of 7.49 up to 8.76 mol/L. I as inhibitor of PDE4 should prove useful in the treatment of airway disorders. Pharmaceutical compns. comprising I are disclosed.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1080903 HCAPLUS Full-text
DOCUMENT NUMBER: 142:56313
TITLE: Preparation of 4,5-dihydro-imidazo[4,5,1-ij]quinolin-6-ones as poly(ADP-ribosyl)transferase (PARP) inhibitors
INVENTOR(S): Weinbrenner, Steffen; Klein, Thomas; Flockerzi, Dieter; **Sterk, Geert Jan; Menge, Wiro M. P. B.**; Brundel, Paulus Johannes Gaurerius; Christiaans, Johannes A. M.
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004108723	A1	20041216	WO 2004-EP51019	20040603

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-12701 A 20030604

OTHER SOURCE(S): MARPAT 142:56313

AB The title compds. (I) (R1 = H, halogen; R2 = morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, Q; R3 = H, C1-4 alkyl, C1-4 alkoxycarbonyl, C1-4 alkylsulfonyl-C1-4 alkyl), and the salts, the N-oxides and the salts of the N-oxides of these compds. are prepared These compds. are useful for treating cancer, inflammation, ischemia/reperfusion injury during organ transplantation surgery, cerebral stroke, myocardial infarct, and diabetes mellitus. Thus, 0.64 g (3.5 mmol) 8-amino-6-fluoro-2,3-dihydro-1H-quinolin-4-one, 0.74 g (3.5 mmol) 4-(4-formylphenyl)piperazine-1-carboxylic acid tert-Bu ester and 0.46 g (4.2 mmol) 1,4-benzoquinone were refluxed in 40 mL ethanol for 4 h to give 4-[4-[8-Fluoro-6-oxo-5,6-dihydroimidazo[4,5,1-ij]quinolin-2- yl]phenyl]piperazine-1-carboxylic acid tert-Bu ester which was dissolved in trifluoroacetic acid and stirred for 1 h at room temperature to give 2-(4-piperazin-1-ylphenyl)-4,5-dihydroimidazo[4,5,1-ij]quinolin-6-one tris(trifluoroacetate).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:182870 HCAPLUS Full-text

DOCUMENT NUMBER: 140:217652

TITLE: Preparation of pyrrolidinedione substituted piperidine-phthalazones as cyclic nucleotide phosphodiesterase-4 (PDE4) inhibitors

INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christiaans, Johannes A. M.; **Menge, Wiro M. P. B.; Sterk, Geert Jan**

PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany

SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018457	A1	20040304	WO 2003-EP8675	20030806

W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW

RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2494613	A1	20040304	CA 2003-2494613	20030806
AU 2003258576	A1	20040311	AU 2003-258576	20030806
EP 1537100	A1	20050608	EP 2003-792257	20030806
EP 1537100	B1	20070425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013330	A	20050614	BR 2003-13330	20030806
CN 1671695	A	20050921	CN 2003-818520	20030806
JP 2006500370	T	20060105	JP 2004-530086	20030806
AT 360627	T	20070515	AT 2003-792257	20030806
IN 2005MN00028	A	20050218	IN 2005-MN28	20050112
MX 2005PA01354	A	20050428	MX 2005-PA1354	20050202
US 2006160813	A1	20060720	US 2005-523412	20051107
US 7220746	B2	20070522		

PRIORITY APPLN. INFO.: EP 2002-17977 A 20020810
WO 2003-EP8675 W 20030806

OTHER SOURCE(S): MARPAT 140:217652

AB 1-(4-Piperidinyl)-4a,5,8,8a-tetrahydro-1H-phthalazin-1-one compds. of formula (I) [R1 and R2 are both H or together form an addnl. bond; R3 = a Ph derivative of formulas Q or Q1; R4 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; R5 = C1-4 alkoxy, C3-7 cycloalkoxy, C3-7 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R6 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; wherein R7 = C1-4 alkyl; R8 = H, C1-4 alkyl; or R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulfur atom; R9 = CO(CH2)n-R10; wherein R10 = 2,5-dioxopyrrolidin-1-yl; n = an integer of 1-4] and the salts of these compds. These compds. are useful in the preparation of pharmaceutical compns. for the treatment of an illness treatable by the administration of a PDE4 inhibitor, in particular airway disorders. Thus, 1-[2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo- 4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]piperidin-1-yl]-2- oxoethyl]pyrrolidine-2,5-dione >. Thus, a mixture of 1 g (4aS,8aR)-2-[1-(2-Chloroethanoyl)piperidin-4-yl]-4-(3,4-dimethoxyphenyl)- 4a,5,8,8a-tetrahydro-2H-phthalazin-1-one, 0.4 g succinimide, 1 g potassium carbonate in 20 mL DMF was stirred for 18 h at room temperature to give, after workup and silica gel chromatog. and crystallization from EtOAc, 1-[2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H- phthalazin-2-yl]piperidin-1-yl]-2-oxoethyl]pyrrolidine-2,5-dione (II). II showed -logIC50(mol/L) of 10.66 against PDE4.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182864 HCAPLUS Full-text
DOCUMENT NUMBER: 140:217651
TITLE: Preparation of piperidinylpyridazinones as inhibitors of phosphodiesterase PDE4 or PDE3/4 inhibitors.
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christiaans, Johannes A. M.; **Menge, Wiro M. P. B.; Sterk, Geert Jan**
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018451	A1	20040304	WO 2003-EP8677	20030806
WO 2004018451	A8	20040506		
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2494650	A1	20040304	CA 2003-2494650	20030806
AU 2003251693	A1	20040311	AU 2003-251693	20030806
EP 1556369	A1	20050727	EP 2003-792259	20030806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005538138	T	20051215	JP 2004-530088	20030806
US 2006167001	A1	20060727	US 2005-523112	20050203
PRIORITY APPLN. INFO.:			EP 2002-17976 A	20020810
			WO 2003-EP8677 W	20030806

OTHER SOURCE(S): MARPAT 140:217651

AB Title compds. [I; R1, R2 = H, alkyl; R3 = Q1, Q2; R4 = (fluoro)alkoxy; R5, R6 = cycloalkoxy, cycloalkylmethoxy, (fluoro)alkoxy; R7 = alkyl; R8 = H, alkyl; R7R8 = atoms to form a 5-7 membered ring optionally interrupted by O, S; R9 = alkyl, SO2R10, COR13, aryl, etc.; R10 = alkyl, 5-dimethylaminonaphthalen-1-yl, thienyl, NR16R17, (substituted) Ph, etc.; R13 = alkyl, carboxyalkyl, Ph, pyridyl, NR16R17, etc.; R16 = H, alkyl, cycloalkyl, cycloalkylmethyl, (substituted) Ph; R17 = alkyl, cycloalkyl, cycloalkylmethyl, (substituted) Ph; NR16R17 = 4-morpholinyl, 1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroazepinyl, (substituted) piperazinyl], were prepared Thus, piperidin-4-ylhydrazine dihydrochloride (preparation given), 4-(3,4-dimethoxyphenyl)-3-methyl-4-oxobutyric acid, and Et3N were refluxed 18 h in PrOH to give 6-(3,4-dimethoxyphenyl)-5-methyl-2- piperidin-4-yl-4,5-dihydro-2H-pyridazin-3-one hydrochloride. I inhibited PDE4 with -log IC50 = 7.17-8.39.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:182863 HCAPLUS Full-text

DOCUMENT NUMBER: 140:235730

TITLE: Preparation of piperidine-N-oxide derivatives as phosphodiesterase 4 inhibitors

INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Brundel, Paulus Johannes Gaurerius; Christiaans, Johannes A. M.; **Menge, Wiro M. P. B.; Sterk, Geert Jan**

PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany

SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018450	A1	20040304	WO 2003-EP8676	20030806
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE,				

DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2494643	A1	20040304	CA 2003-2494643	20030806
AU 2003260371	A1	20040311	AU 2003-260371	20030806
EP 1542987	A1	20050622	EP 2003-792258	20030806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005538137	T	20051215	JP 2004-530087	20030806
US 2006166995	A1	20060727	US 2005-523110	20050203
PRIORITY APPLN. INFO.:			EP 2002-17978 A	20020810
			WO 2003-EP8676 W	20030806

OTHER SOURCE(S): MARPAT 140:235730

AB The 1,2-dihydro-2-(1-oxidopiperidin-4-yl)phthalazin-2-one derivs. [I; R1, R2 = H, C1-4 alkyl; or R1 and R2 together and with inclusion of the two carbon atoms, to which they are bonded, form a group selected from cyclohexane-1,2-diyl or 4-cyclohexene-1,2-diyl; R3 = a Ph derivative of formulas Q or Q1; R4 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; R5 = C1-8 alkoxy, C3-7 cycloalkoxy, C3-7 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R6 = C1-4 alkoxy, C3-5 cycloalkoxy, C3-5 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R7 = C1-4 alkyl; R8 = H, C1-4 alkyl; or wherein R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulfur atom; R9 = (CH2)mSO2R10, (CH2)nCOR11, -(CH2)p-Z-(CH2)q-R14; wherein R10, R11 = N(R12)R13; R12, R13 = H, C1-7 alkyl, C3-7 cycloalkyl, C3-7 cycloalkylmethyl; or NR12R13 together forms a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl- or a 1-hexahydroazepinyl ring; Z = a bond, O, CO, CONH, NHCO, SO2; R14 = H, OH, C1-4 alkoxy, hydroxy-C2-4 alkoxy, C1-4 alkoxy-C1-4 alkoxy, C1-4 alkoxycarbonyl, (un)substituted aminocarbonyl, etc.; m, n, p, q = an integer from 1 to 4] and the salts of these compds. are prepared These compds. are novel effective PDE4 inhibitors and useful for treating an illness treatable by the administration of a PDE4 inhibitor in a patient, in particular airway disorders. Thus, a solution of 1.2 g 2-[4-[(4aS,8aR)-4-(3,4-Dimethoxy)phenyl]-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]piperidin- 1-yl-2H-acetamide hydrochloride in 100 mL CH2Cl2 was washed with aqueous saturated NaHCO3 solution, dried over anhydrous MgSO4, cooled to 0°, treated with 0.6 g 3-chloroperbenzoic acid (70% purity), and stirred for 60 min to give, after workup and silica gel chromatog. and crystallization from EtOAc, 2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-1-oxypiperidin-1-yl]acetamide (II). II and 2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H- phthalazin-2-yl]-1-oxypiperidin-1-yl]-N-isopropylacetamide showed -logIC50 (mol/L) of 8.31 and 9.3, resp., against PDE4.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:182862 HCAPLUS Full-text

DOCUMENT NUMBER: 140:217665

TITLE: Preparation of piperidinylphthalazinone derivatives as PDE4 inhibitors

INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christiaans, Johannes A. M.; **Menge, Wiro M. P. B.; Sterk, Geert Jan**; Weinbrenner, Steffen

PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany

SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018449	A1	20040304	WO 2003-EP8673	20030806
WO 2004018449	A8	20040506		
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
AU 2003255376	A1	20040311	AU 2003-255376	20030806
PRIORITY APPLN. INFO.:			EP 2002-17979 A	20020810
			WO 2003-EP8673 W	20030806

OTHER SOURCE(S): MARPAT 140:217665

AB The title compound I [R1, R2 = H or together form an addnl. bond; R3 = benzene derivative Q1 or Q2; R4 = (substituted)arylsulfonyl; R5 = alkoxy or polyfluoroalkyoxy; R6, R7 = (cyclo)alkoxy, cycloalkylmethoxy, or polyfluoroalkyoxy; R8 = alkyl; R9 = H or alkyl; or R7 and R8 together with the 2 intervening C atoms form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by O or S] were prepared as PDE4 inhibitors. Thus, reaction of (4aS,8aR)-4-(3,4-dimethoxyphenyl)-2- piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (preparation given) with naphthalene-1-sulfonyl chloride gave compound II. The prepared compds. inhibited PDE4 with -log(IC50) ≥ 8.8.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182711 HCAPLUS Full-text
DOCUMENT NUMBER: 140:235729
TITLE: Preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors
INVENTOR(S): **Sterk, Geert Jan**; Hatzelmann, Armin; Marx, Degenhard; Kley, Hans-Peter; **Menge, Wiro M. P. B.**
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017974	A1	20040304	WO 2003-EP8724	20030806
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2494634	A1	20040304	CA 2003-2494634	20030806
AU 2003260376	A1	20040311	AU 2003-260376	20030806
EP 1556049	A1	20050727	EP 2003-792267	20030806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005538140	T	20051215	JP 2004-530096	20030806
AT 360627	T	20070515	AT 2003-792257	20030806
US 2006094710	A1	20060504	US 2005-523111	20051003
PRIORITY APPLN. INFO.:			EP 2002-17977 A	20020810
			WO 2003-EP8724 W	20030806

OTHER SOURCE(S): MARPAT 140:235729

AB Title compds. I [R1-2 = H, alkyl, etc.; R3 = substituted Ph, etc.; R9 = naphthyl, pyrazinyl, pyridazinyl, etc.] are prepared For instance, (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H- phthalazin-1-one hydrochloride (preparation given) is reacted with methanesulfonylacetic acid (CH2Cl2, Et3N) to give II. Compds. of the invention have pIC50 ≥ 9 for the PDE4 receptor. I are useful for the treatment of airway disorders.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:276736 HCAPLUS Full-text

DOCUMENT NUMBER: 138:287688

TITLE: Tetrahydrothiopyran **phthalazinone** derivatives useful as **PDE4 inhibitors**

INVENTOR(S): **Sterk, Geert Jan**

PATENT ASSIGNEE(S): Altana Pharma AG, Germany

SOURCE: U.S., 12 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6544993	B1	20030408	US 2002-110397	20020412
WO 2001030777	A1	20010503	WO 2000-EP10445	20001024
W: AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 2003166655	A1	20030904	US 2003-372243	20030225
US 6846821	B2	20050125		
PRIORITY APPLN. INFO.:			AT 1999-121243 A	19991025
			US 2000-203950P P	20000512
			WO 2000-EP10445 W	20001024
			EP 1999-121243 A	19991025
			US 2002-110397 A1	20020412

OTHER SOURCE(S): MARPAT 138:287688

AB Title compds. I are novel, effective PDE4 inhibitors [in which: R1, R2 = H; or R1R2 = pi bond; A = S (sulfur), S(O) (sulfoxide), or S(O)2 (sulfone); Ar = benzene derivative Q1 or Q2; R3 = halo, C1-4 alkoxy or polyfluoroalkoxy; R4 = halo, C1-8 alkoxy, C1-4 polyfluoroalkoxy, C3-7 cycloalkoxy, C3-7 cycloalkylmethoxy; R5 = halo, C1-4 alkoxy, C1-4 polyfluoroalkoxy, C3-5 cycloalkoxy, C3-5 cycloalkylmethoxy; R6 = C1-4 alkyl; R7 = H, C1-4 alkyl; or R6 and R7 together with the 2 intervening C atoms form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by O or S; and salts; with the exclusion of A = S, Ar = Q1, and both of R3 and R4 = other than halo]. Ten preparative examples are given. For instance, cyclocondensation of cis-2-(2,3-dihydro-2,2-dimethyl-7-methoxybenzofuran-4-carbonyl)-1,2,3,6-tetrahydrobenzoic acid with 4-hydrazinotetrahydrothiopyran-HCl in refluxing

pyridine gave racemic title compound II. This compound inhibited PDE 4 in vitro with -log(IC50) = 9.34, and 7 other I gave values of 8.02 to 9.43.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:832801 HCAPLUS Full-text
DOCUMENT NUMBER: 137:337906
TITLE: Preparation of phthalazinones as phosphodiesterase 4/7 inhibitors.
INVENTOR(S): Hatzelmann, Armin; Marx, Degenhard; Steinhilber, Wolfram; **Sterk, Geert Jan**
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085906	A2	20021031	WO 2002-EP4438	20020423
WO 2002085906	A3	20021219		
W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2445233	A1	20021031	CA 2002-2445233	20020423
AU 2002317733	A1	20021105	AU 2002-317733	20020423
EP 1385848	A2	20040204	EP 2002-747291	20020423
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300514	A	20040216	EE 2003-514	20020423
HU 2003003998	A2	20040528	HU 2003-3998	20020423
HU 200303998	A3	20070328		
CN 1503792	A	20040609	CN 2002-808742	20020423
BR 2002009149	A	20040713	BR 2002-9149	20020423
JP 2004526789	T	20040902	JP 2002-583433	20020423
NZ 529221	A	20050429	NZ 2002-529221	20020423
MX 2003PA09583	A	20040212	MX 2003-PA9583	20031020
US 2004127707	A1	20040701	US 2003-475657	20031023
US 7186710	B2	20070306		
NO 2003004773	A	20031210	NO 2003-4773	20031024
BG 108294	A	20040930	BG 2003-108294	20031027
ZA 2003008930	A	20040609	ZA 2003-8930	20031117
IN 2003MN01079	A	20050429	IN 2003-MN1079	20031124
PRIORITY APPLN. INFO.:			EP 2001-110228 A	20010425
			WO 2002-EP4438 W	20020423

OTHER SOURCE(S): MARPAT 137:337906

AB Title compds. (I; R1 = alkoxy, fluoroalkoxy; R2 = F, Br, Cl; R3, R4 = H; R3R4 = bond; R5 = alkyl, cycloalkyl, cycloalkylmethyl, alkenyl, alkynyl, phenylalkenyl, polycycloalkyl, naphthyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, etc.), were prepared Thus, cis-4-(3-chloro-4-methoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (preparation given) was stirred 16 h with morpholine-4-carbonyl chloride in pyridine to give cis-4-(3-chloro-4-methoxyphenyl)-2-[1-(1-morpholin-4-ylmethanoyl)piperidin- 4-yl]-

4a,5,8,8a-tetrahydro-2H-phthalazin-1-one. The latter inhibited PDE4 and PDE7 with -log IC50 = 8.64 and 7.64, resp.

L38 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:637671 HCAPLUS Full-text
DOCUMENT NUMBER: 137:185496
TITLE: Preparation of piperidinyl benzopyridazine derivatives as PDE4 inhibitors for treatment of airway disorders
INVENTOR(S): Hatzelmann, Armin; Bundschuh, Daniela; Kley, Hans-peter; Timmerman, Hendrik; Christiaans, Johannes A. M.; Grundler, Gerhard; Gutterer, Beate; **Sterk, Geert Jan**
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik Gmbh, Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064584	A1	20020822	WO 2002-EP1547	20020214
W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2438520	A1	20020822	CA 2002-2438520	20020214
AU 2002234634	A1	20020828	AU 2002-234634	20020214
AU 2002234634	B2	20070726		
EE 200300311	A	20031015	EE 2003-311	20020214
EP 1362044	A1	20031119	EP 2002-701277	20020214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003003193	A2	20031229	HU 2003-3193	20020214
HU 200303193	A3	20070828		
BR 2002007278	A	20040210	BR 2002-7278	20020214
JP 2004518727	T	20040624	JP 2002-564515	20020214
CN 1524080	A	20040825	CN 2002-805038	20020214
NZ 527424	A	20050225	NZ 2002-527424	20020214
IN 2003MN00668	A	20050211	IN 2003-MN668	20030701
US 2004067946	A1	20040408	US 2003-467832	20030813
US 6953853	B2	20051011		
NO 2003003618	A	20031015	NO 2003-3618	20030814
MX 2003PA07310	A	20031204	MX 2003-PA7310	20030815
BG 108124	A	20040831	BG 2003-108124	20030821
ZA 2003006815	A	20040617	ZA 2003-6815	20030901
US 2005234062	A1	20051020	US 2005-143721	20050603
US 7179810	B2	20070220		
US 2007129373	A1	20070607	US 2006-647191	20061229

PRIORITY APPLN. INFO.:		
EP 2001-103496	A	20010215
WO 2002-EP1547	W	20020214
US 2003-467832	A1	20030813
US 2005-143721	A1	20050603

OTHER SOURCE(S): MARPAT 137:185496
AB Piperidinyl benzopyridazine derivs. [I; wherein R1 and R2 = H, or together form an addnl. bond; R3 = substituted benzene, benzopyran derivative; R4 =

(C1-C4)alkoxy, optionally substituted with fluorine] were prepared Thus, to a solution of (4aS,8aR)-4-(3,4-diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (synthetic preparation given) and p-TsCl in pyridine is stirred to give (4aS,8aR)-4-(3,4-diethoxyphenyl)-2- [1-(toluene-4-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin- 1-one. The prepared compds. are effective PDE4 inhibitors useful in the treatment of airway disorders.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:832781 HCAPLUS Full-text
DOCUMENT NUMBER: 137:337905
TITLE: Preparation of piperazino **phthalazinone** derivatives and their use as **PDE4 inhibitors**
INVENTOR(S): Hatzelmann, Armin; Bundschuh, Daniela; Barsig, Johannes; Kley, Hans-Peter; Grundler, Gerhard; Schmidt, Beate; **Sterk, Geert Jan**
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085885	A1	20021031	WO 2002-EP4494	20020424
W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2445236	A1	20021031	CA 2002-2445236	20020424
AU 2002315311	A1	20021105	AU 2002-315311	20020424
EP 1385838	A1	20040204	EP 2002-740498	20020424
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300513	A	20040216	EE 2003-513	20020424
HU 2003003469	A2	20040301	HU 2003-3469	20020424
CN 1505624	A	20040616	CN 2002-808772	20020424
BR 2002009076	A	20040810	BR 2002-9076	20020424
JP 2004526785	T	20040902	JP 2002-583412	20020424
NZ 529363	A	20050826	NZ 2002-529363	20020424
BG 108187	A	20040930	BG 2002-108187	20020923
US 2004132721	A1	20040708	US 2003-475656	20031023
US 7022696	B2	20060404		
MX 2003PA09806	A	20040129	MX 2003-PA9806	20031024
NO 2003004804	A	20031229	NO 2003-4804	20031027
ZA 2003008931	A	20040609	ZA 2003-8931	20031117
IN 2003MN01078	A	20050218	IN 2003-MN1078	20031124
JP 2006096766	A	20060413	JP 2005-336182	20051121

PRIORITY APPLN. INFO.:
EP 2001-110227 A 20010425
JP 2002-583412 A3 20020424
WO 2002-EP4494 W 20020424

OTHER SOURCE(S): MARPAT 137:337905

AB Piperazino phthalazinone derivs. [I; wherein R1, R2 = H, or together form an addnl. bond; R3 = (substituted) aryl, (substituted) benzofuran; A = a bond, CH2; X = C(O), S(O)2; n = 1, 2; R4 = alkylcarbonyl, aryl, hetaryl, phenylprop-1-en-3-yl, 1-methylpiperidin-4-yl] were prepared For example, (4aS,8aR)-4-(3,4-diethoxyphenyl)-2-{4-[1-(4-phenylpiperazin-1- yl)methanoyl]phenyl}-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride was prepared by a multistep synthetic procedure. The prepared compds. are useful as PDE4 inhibitors and, in particular, in the treatment of respiratory tract inflammation disorders.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:904118 HCAPLUS Full-text
DOCUMENT NUMBER: 136:37625
TITLE: Preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Bundschuh, Daniela; Eltze, Manfrid; Van der Laan, Yvonne; Timmermann, Hendrik; Christiaans, Johannes; Brundel, Paulus; **Sterk, Geert**
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany; Byk Nederland B.V.
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094319	A1	20011213	WO 2001-EP6230	20010601
W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2411351	A1	20011213	CA 2001-2411351	20010601
EP 1296956	A1	20030402	EP 2001-936419	20010601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011440	A	20030603	BR 2001-11440	20010601
JP 2003535850	T	20031202	JP 2002-501869	20010601
HU 2003001240	A2	20031229	HU 2003-1240	20010601
NZ 522882	A	20040730	NZ 2001-522882	20010601
IN 2002MN01591	A	20050318	IN 2002-MN1591	20021111
ZA 2002009598	A	20030729	ZA 2002-9598	20021126
NO 2002005811	A	20030204	NO 2002-5811	20021203
MX 2002PA12042	A	20040819	MX 2002-PA12042	20021205
US 2003195215	A1	20031016	US 2003-296411	20030402
US 6933296	B2	20050823		

PRIORITY APPLN. INFO.: EP 2000-111795 A 20000605
WO 2001-EP6230 W 20010601

OTHER SOURCE(S): MARPAT 136:37625

AB The title compds. [I; Ar1 = substituted Ph, dihydrobenzofuranyl; R6, R7 = H, alkyl; or R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form II-V; A = CmH2mYXCnH2n, YXCmH2mZCnH2n; X = a bond, O, S, etc.; Y = a bond, phenylene, cycloalkylene, etc.; Z = O, S, SO2, etc.; m = 0-4; n = 1-4; R8 = H, alkyl; Ar2 = 8-hydroxy-1H-quinolin-2-on-5-yl,

substituted Ph], useful as novel effective bronchial therapeutics, were prepared The general procedures for preparation of compds. I such as (cis)-VI.fumarate were described. Biol. data for compds. I were given.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:613874 HCAPLUS Full-text
DOCUMENT NUMBER: 131:228728
TITLE: Preparation of arylphthalazinones as phosphodiesterase III/IV inhibitors.
INVENTOR(S): Hatzelmann, Armin; Boss, Hildegard; Hafner, Dietrich; Beume, Rolf; Kley, Hans-Peter; Van Der Laan, Ivonne Johanna; Timmerman, Hendrik; **Sterk, Geert Jan** ; Van Der Mey, Margaretha
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany; Van Der Mey, Margaretha
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947505	A1	19990923	WO 1999-EP1413	19990304
W: AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2323771	A1	19990923	CA 1999-2323771	19990304
AU 9933284	A	19991011	AU 1999-33284	19990304
EP 1070056	A1	20010124	EP 1999-914474	19990304
EP 1070056	B1	20040630		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002506856	T	20020305	JP 2000-536702	19990304
AT 270278	T	20040715	AT 1999-914474	19990304
PT 1070056	T	20041130	PT 1999-914474	19990304
ES 2224628	T3	20050301	ES 1999-914474	19990304
US 6255303	B1	20010703	US 2000-623477	20000913
PRIORITY APPLN. INFO.:			EP 1998-104643 A	19980314
			WO 1999-EP1413 W	19990304

OTHER SOURCE(S): MARPAT 131:228728
AB Title compds. [I; R1 = OH, alkoxy, fluoroalkoxy; R2 = OH, halo, alkoxy, cycloalkoxy, cycloalkylmethoxy, fluoroalkoxy; R3, R4 = H; R3R4 = bond; X, Y = bond; or X = (CH2)n and Y = O, S, CO2, CONH, SO2NH; or X = phenylene and Y = CO2, CONH, SO2NH; A = S, CHR51; R51, R52 = H, alkyl; R51R52 = bond], were prepared Thus, cis-4-[4-(3,4-dimethoxyphenyl)-1-oxo-4a,5,8,8a- tetrahydro-2H-phthalazin-2-yl]benzoic acid (preparation given) was stirred with PCl5 in CH2Cl2; the residue was stirred with 6-(4-aminophenyl)-2H- pyridazin-3-one and 4-dimethylaminopyridine in THF to give cis-N-[4-(6-oxo-1,6-dihydropyridazin-3-yl)phenyl]-4-[4-(3,4- dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]benzamide. The latter inhibited PDE4 with -log IC50 = 9.08.
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:519555 HCAPLUS Full-text
DOCUMENT NUMBER: 131:130001
TITLE: **Phthalazinones** useful as PDE 4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Boss, Hildegard; Hafner, Dietrich; Beume, Rolf; Kley, Hans-Peter; **Sterk, Geert Jan**; Timmerman, Hendrik
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 934933	A1	19990811	EP 1998-102032	19980206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			EP 1998-102032	19980206

OTHER SOURCE(S): MARPAT 131:130001
AB Phthalazinones I [R1 = (fluoro)alkoxy; R2 = halo, (cyclo)alkoxy, cycloalkylmethoxy, fluoroalkoxy; R3 = -CnH2nCOR4; R4 = (un)substituted Ph, naphthyl, pyridyl; n = 1-4] are prepared I are inhibitors of PDE4, and are thus useful as bronchial therapeutics, and for the treatment of dermatoses. Fifteen examples were prepared For instance, N-alkylation of 4-(3,4-dimethoxyphenyl)-2H-phthalazin-1-one by ω-bromo-2- methoxyacetophenone in the presence of K2CO3 gave title compound II. The latter compound had pIC50 of 7.52 for inhibition of PDE4 in vitro.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:509189 HCAPLUS Full-text
DOCUMENT NUMBER: 129:136174
TITLE: Preparation of arylphthalazinones as inhibitors of cyclic nucleotide phosphodiesterase.
INVENTOR(S): Van Der Mey, Margaretha; Van Der Laan, Ivonne Johanna; Timmerman, Hendrik; Hatzelmann, Armin; Boss, Hildegard; Hafner, Dietrich; Beume, Rolf; Kley, Hans-Peter; **Sterk, Geert Jan**
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831674	A1	19980723	WO 1998-EP124	19980112
W: AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IL, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, US, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2276455	A1	19980723	CA 1998-2276455	19980112
CA 2276455	C	20061031		
AU 9858629	A	19980807	AU 1998-58629	19980112
AU 735934	B2	20010719		

EP 971901	A1	20000119	EP 1998-901959	19980112
EP 971901	B1	20030226		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
EE 9900274	A	20000215	EE 1999-274	19980112
EE 3968	B1	20030217		
BR 9806752	A	20000314	BR 1998-6752	19980112
NZ 336573	A	20001027	NZ 1998-336573	19980112
JP 2001508078	T	20010619	JP 1998-533635	19980112
IL 130659	A	20020725	IL 1998-130659	19980112
AT 233247	T	20030315	AT 1998-901959	19980112
SK 283270	B6	20030401	SK 1999-951	19980112
PT 971901	T	20030731	PT 1998-901959	19980112
ES 2193508	T3	20031101	ES 1998-901959	19980112
CN 1127487	B	20031112	CN 1998-803169	19980112
CZ 293815	B6	20040818	CZ 1999-2533	19980112
PL 189418	B1	20050831	PL 1998-334561	19980112
NO 9903301	A	19990910	NO 1999-3301	19990702
NO 313137	B1	20020819		
US 6103718	A	20000815	US 1999-341135	19990714
HK 1024692	A1	20030620	HK 2000-103993	20000630
PRIORITY APPLN. INFO.:			EP 1997-100488 A	19970115
			WO 1998-EP124 W	19980112

OTHER SOURCE(S): MARPAT 129:136174

AB Title compds. [I; R1 = alkoxy, fluoroalkoxy; R2 = alkoxy, cycloalkoxy, cycloalkylmethoxy, fluoroalkoxy; R3, R4 = H, or R3R4 = bond; R5 = R6, (CH2)mR7, (CH2)nCOR8, CH(R9)2, (CH2)pAr; R6 = H, alkyl, cycloalkyl, cycloalkylmethyl, alkenyl, alkynyl, naphthyl, phenylalkenyl, pyridyl, pyrazinyl, indanyl, etc.; R7 = OH, halo, cyano, NO2, ONO2, CO2H, PhO, alkoxy, cycloalkoxy, alkylcarbonylamino, etc.; R8 = (substituted) Ph, naphthyl, phenanthryl, anthracenyl; R9 = (CH2)qPh; Ar = naphthyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, quinazolinyl, cinnolinyl, isoquinolinyl, imidazolyl, pyrazolyl, oxazolyl, thiazolyl, furyl, thienyl, pyrrolyl, (substituted) Ph, etc.; m = 1-8; n = 1-4; p = 1-6; q = 0-2], were prepared Thus, cis-4-(3,4-dimethoxyphenyl)-2-propyl-4a,5,6,7,8,8a- hexahydro-2H-phthalazin-1-one (preparation outlined) inhibited PDE 4 with -log IC50 >7.5.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 21 OF 24 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 2001437055 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11472205

TITLE: Novel selective **PDE4 inhibitors.** 1. Synthesis, structure-activity relationships, and molecular modeling of 4-(3,4-dimethoxyphenyl)-2H-phthalazin-1-ones and analogues.

AUTHOR: Van der Mey M; Hatzelmann A; Van der Laan I J; **Sterk G J**; Thibaut U; Timmerman H

CORPORATE SOURCE: Leiden/Amsterdam Center for Drug Research, Division of Medicinal Chemistry, Department of Pharmacochemistry, Vrije Universiteit, De Boelelaan 1083, 1081 HV Amsterdam.. mmeijJ@rnc.vu.nl

SOURCE: Journal of medicinal chemistry, (2001 Aug 2) Vol. 44, No. 16, pp. 2511-22.
Journal code: 9716531. ISSN: 0022-2623.

PUB. COUNTRY: United States

DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20 Aug 2001
Last Updated on STN: 20 Aug 2001
Entered Medline: 16 Aug 2001

AB A number of 6-(3,4-dimethoxyphenyl)-4,5-dihydro-2H-**pyridazin** -3-ones and a novel series of 4-(3,4-dimethoxyphenyl)-2H-phthalazin-1-ones were prepared and tested on the cGMP-inhibited phosphodiesterase (PDE3) and cAMP-specific phosphodiesterase (PDE4) enzymes. All tested compounds were found to specifically inhibit PDE4 except for **pyridazinone** 3b, which showed moderate PDE4 (pIC(50) = 6.5) as well as PDE3 (pIC(50) = 6.6) inhibitory activity. In both the **pyridazinone** and phthlazinone series it was found that N-substitution is beneficial for **PDE4 inhibition**, whereas in the **pyridazinone** series it also accounts for PDE4 selectivity. In the **phthalazinone** series, the cis-4a,5,6,7,8,8a- hexahydrophthalazinones and their corresponding 4a,5,8,8a-tetrahydro analogues showed potent **PDE4 inhibitory** potency (10/11c,d: pIC(50) = 7.6-8.4). A molecular modeling study revealed that the cis-fused cyclohexa(e)ne rings occupy a region in space different from that occupied by the other fused (un)saturated hydrocarbon rings applied; we therefore assume that the steric interactions of these rings with the binding site play an important role in enzyme inhibition.

L38 ANSWER 22 OF 24 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:220741 BIOSIS Full-text
DOCUMENT NUMBER: PREV200700219092
TITLE: **Phthalazinones.**
AUTHOR(S): Anonymous; **Sterk, Geert Jan** [Inventor]
CORPORATE SOURCE: Stadhouderslaan, Netherlands
ASSIGNEE: Altana Pharma AG
PATENT INFORMATION: US 07186710 20070306
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (MAR 6 2007)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 28 Mar 2007
Last Updated on STN: 28 Mar 2007

AB The compounds of formula I in which R1, R2, R3, R4 and R5 have the meanings as given in the description are PDE4/7 inhibitors.

L38 ANSWER 23 OF 24 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2007:180646 BIOSIS Full-text
DOCUMENT NUMBER: PREV200700173989
TITLE: **Phthalazinone**-piperidino-derivatives as **PDE4 inhibitors.**
AUTHOR(S): Anonymous; Grundler, Gerhard [Inventor]; Schmidt, Beate [Inventor]; **Sterk, Geert Jan** [Inventor]
CORPORATE SOURCE: Constance, Germany
ASSIGNEE: Altana Pharma AG
PATENT INFORMATION: US 07179810 20070220
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (FEB 20 2007)
CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Mar 2007
Last Updated on STN: 7 Mar 2007

AB The compounds of formula I in which the given substituents have the meanings as given in the description, are novel effective **PDE4 inhibitors**.

L38 ANSWER 24 OF 24 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:321130 BIOSIS Full-text
DOCUMENT NUMBER: PREV200400324946
TITLE: **Phthalazinone** derivatives as **PDE4 inhibitors.**
AUTHOR(S): **Sterk, Geert Jan** [Inventor, Reprint Author]
CORPORATE SOURCE: Utrecht, Netherlands
ASSIGNEE: Altana Pharma AG, Constance, Germany
PATENT INFORMATION: US 6756371 20040629
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 29 2004) Vol. 1283, No. 5. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Jul 2004
Last Updated on STN: 21 Jul 2004

AB The compounds of formula (I) in which R1, R2, A, B and Ar have the meanings as given in the description are novel effective **PDe4 inhibitors** ##STR1##

***** QUERY RESULTS *****

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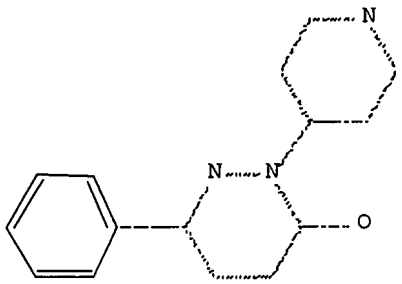

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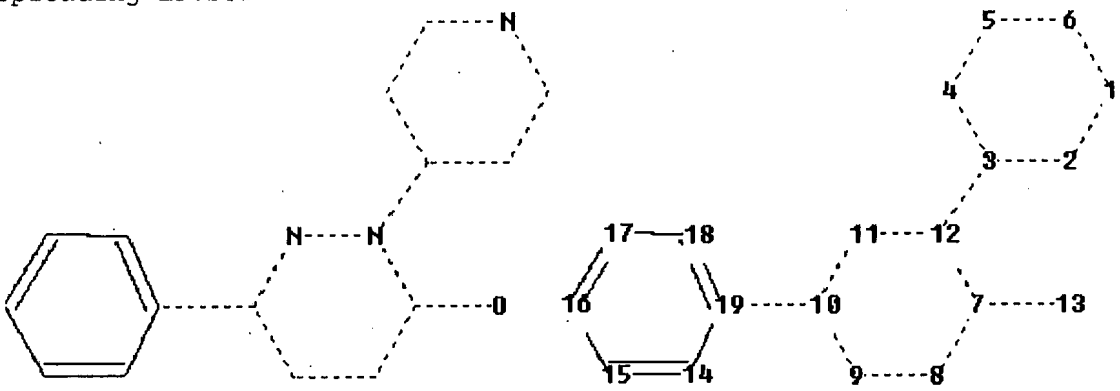


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ring bonds :
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16
16-17  17-18  18-19
exact/norm bonds :
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normalized bonds :
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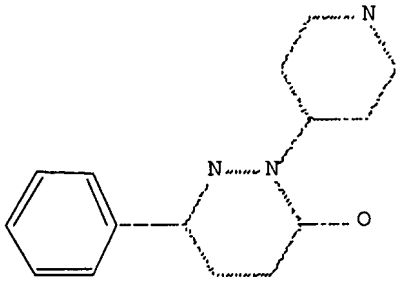


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L18  ANSWER 1 OF 18  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:823689  HCAPLUS  Full-text
DOCUMENT NUMBER:          143:229869
TITLE:                    Preparation of phthalazinone derivatives as PDE4
                          inhibitors
INVENTOR(S):              Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard;
                          Kley, Hans-Peter; Christiaans, Johannes A. M.; Menge,
                          Wiro M. P. B.; Sterk, Geert Jan
PATENT ASSIGNEE(S):       Altana Pharma A.-G., Germany
SOURCE:                   PCT Int. Appl., 57 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
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LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005075457	A1	20050818	WO 2005-EP50417	20050201 <--
WO 2005075457	A8	20060302		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

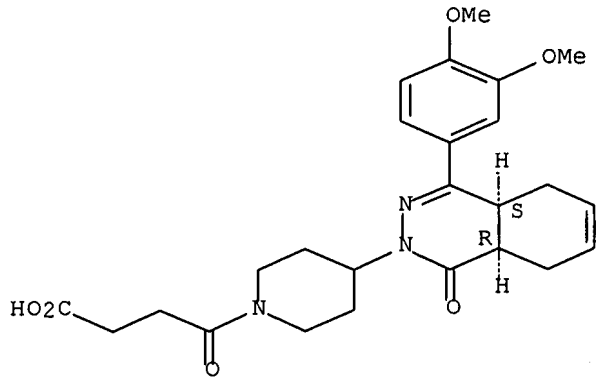
EP 1720854	A1	20061115	EP 2005-701632	20050201 <--

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: EP 2004-2423 A 20040204 <--
WO 2005-EP50417 W 20050201

OTHER SOURCE(S): CASREACT 143:229869; MARPAT 143:229869
ED Entered STN: 19 Aug 2005
AB Title compds. I [R1 and R2 are both H or together from an addnl. bond; R3 = (un)substituted phenyl; R4 = OH, alkoxy, NHR5, etc.; R5 = OH, alkoxy or alkoxyalkyl; n = 0, 2, 3, or 4] and their pharmaceutically acceptable salts, are prepared and disclosed as PDE4 inhibitors. Thus, e.g., II was prepared by coupling of (4aS,8aR)-4-(3,4-dimethoxy-phenyl)-2-piperidin-4-yl- 4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (preparation given) with succinic anhydride. The inhibitory activity of I was evaluated using two different methods utilizing cAMP and it was revealed that compds. of the invention displayed -logIC50 values in the range of 8.4 up to 10.4 mol/L. I as inhibitor of PDE4 should prove useful in the treatment of airway disorders. Pharmaceutical compns. comprising I are disclosed.
IT **862462-47-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of phthalazinone derivs. as PDE4 inhibitors)
RN 862462-47-3 HCAPLUS
CN 1-Piperidinebutanoic acid, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-γ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



IT **862462-48-4P 862462-50-8P 862462-51-9P**
862462-53-1P 862462-54-2P 862462-55-3P
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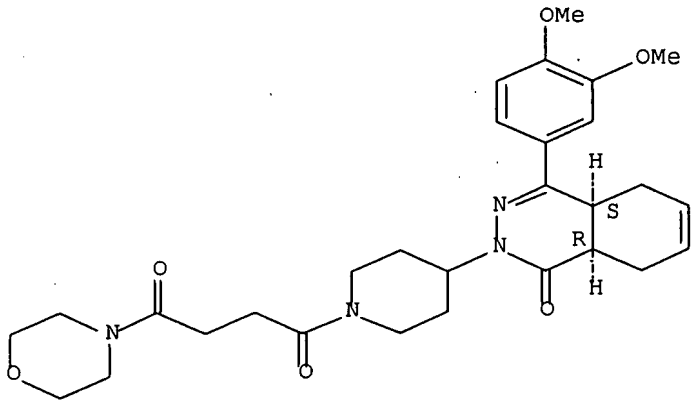
862462-59-7P 862462-60-0P 862462-61-1P
862462-62-2P 862462-63-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phthalazinone derivs. as PDE4 inhibitors)

RN 862462-48-4 HCAPLUS

CN Morpholine, 4-[4-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-1,4-dioxobutyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 862462-50-8 HCAPLUS

CN Piperazine, 1-[4-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-1,4-dioxobutyl]-4-methyl-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

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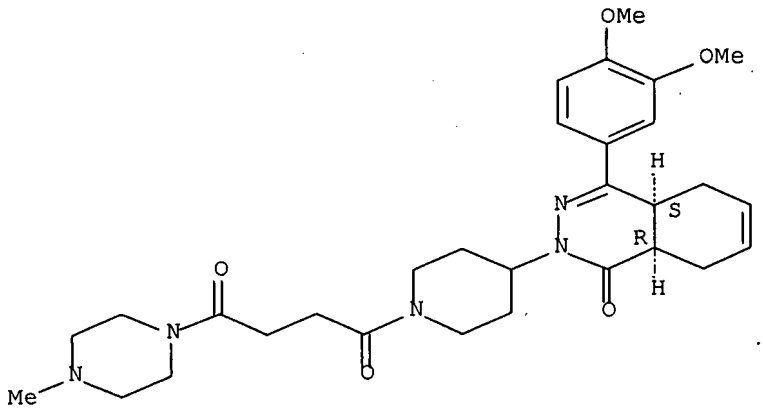
CRN 862462-49-5
CMF C30 H41 N5 O5

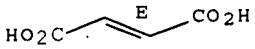
Absolute stereochemistry.



CM 2

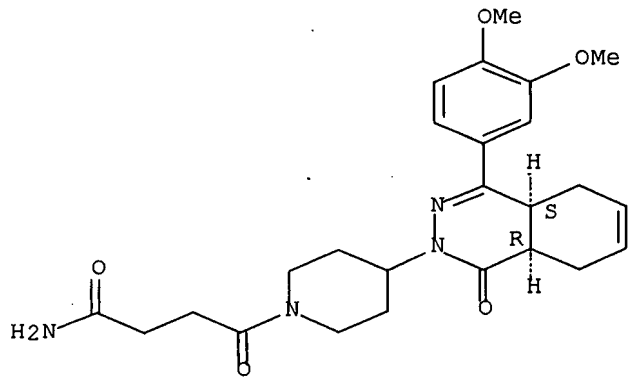
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 862462-51-9 HCAPLUS
CN 1-Piperidinebutanamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-γ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



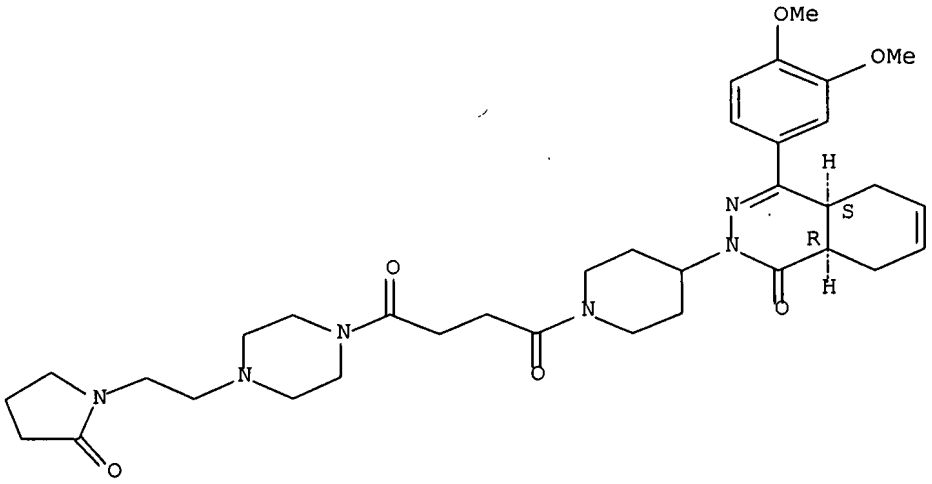
RN 862462-53-1 HCAPLUS
CN Piperazine, 1-[4-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-

tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-1,4-dioxobutyl]-4-[2-(2-oxo-1-pyrrolidinyl)ethyl]-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

CM 1

CRN 862462-52-0
CMF C35 H48 N6 O6

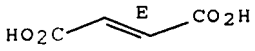
Absolute stereochemistry.



CM 2

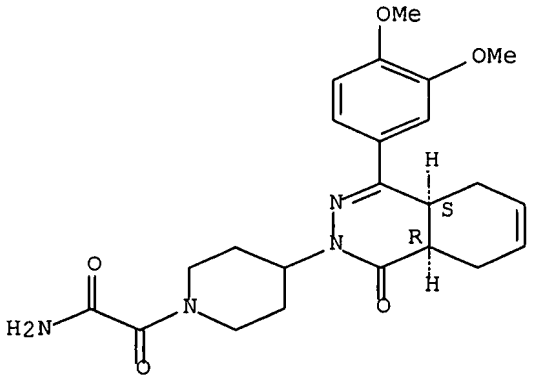
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



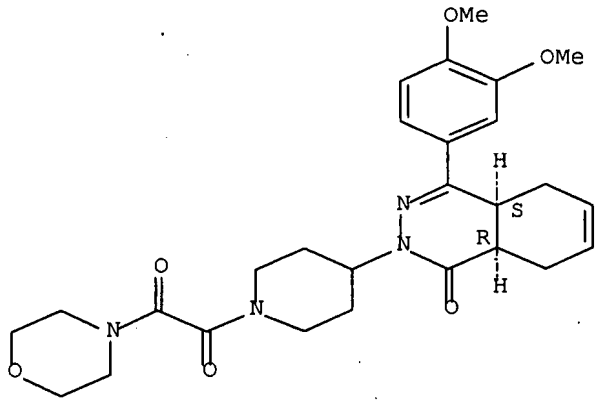
RN 862462-54-2 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-α-oxo- (CA INDEX NAME)

Absolute stereochemistry.



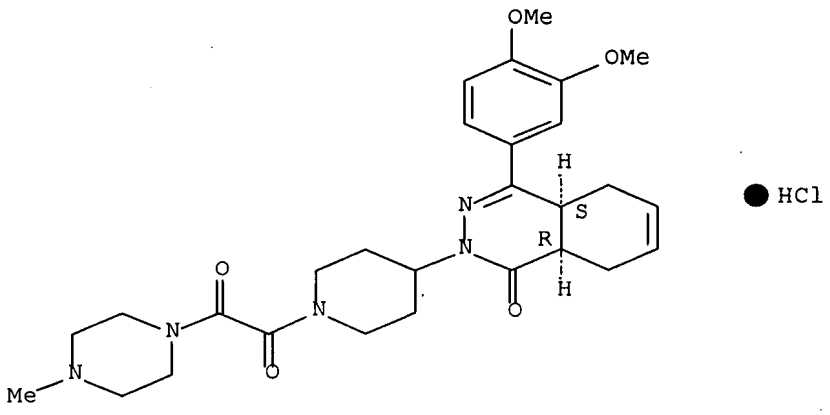
RN 862462-55-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



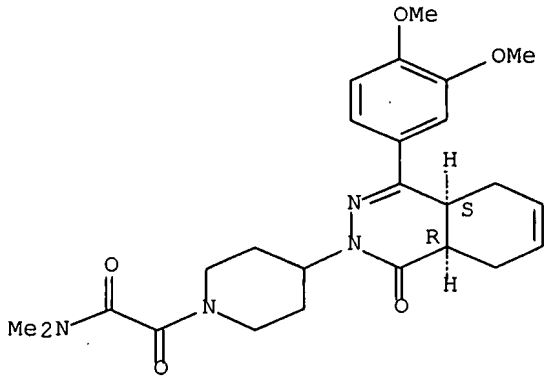
RN 862462-56-4 HCAPLUS
CN Piperazine, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



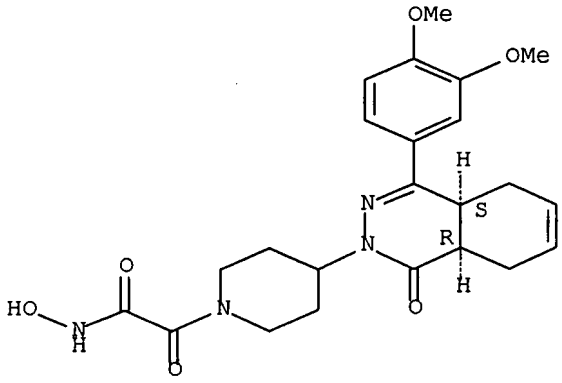
RN 862462-57-5 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N,N-dimethyl-α-oxo- (CA INDEX NAME)

Absolute stereochemistry.



RN 862462-58-6 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-hydroxy-α-oxo- (CA INDEX NAME)

Absolute stereochemistry.



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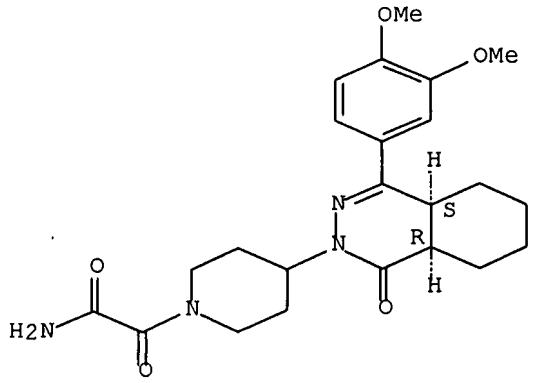
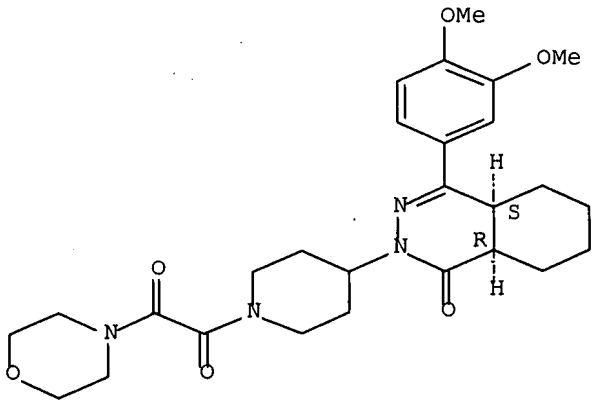
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-α-oxo- (CA INDEX NAME)

Absolute stereochemistry.



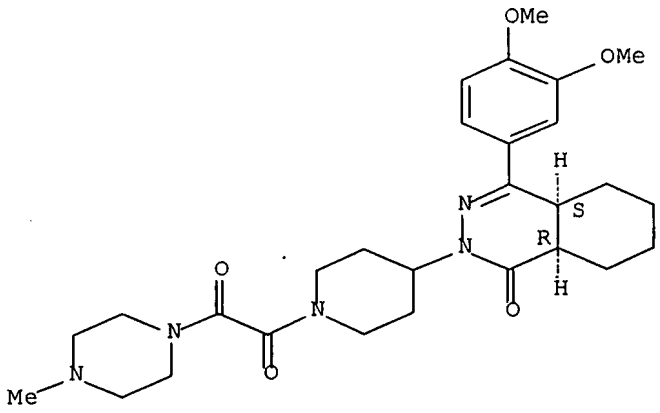
RN 862462-60-0 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



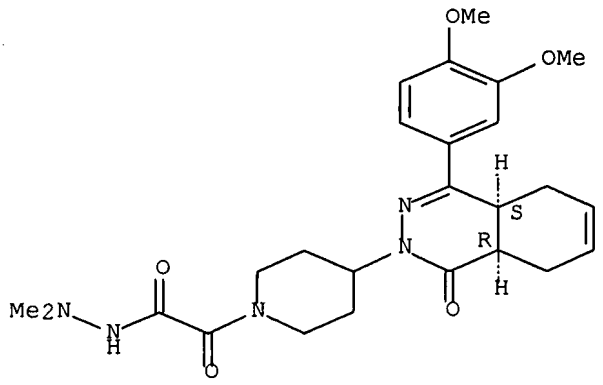
RN 862462-61-1 HCAPLUS
CN Piperazine, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]-4-methyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



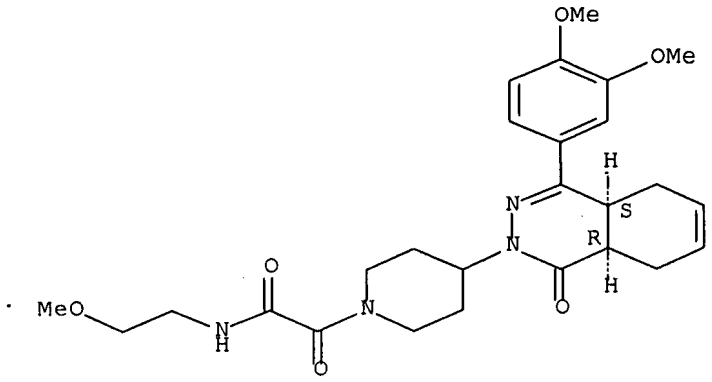
RN 862462-62-2 HCAPLUS
CN 1-Piperidineacetic acid, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-α-oxo-, 2,2-dimethylhydrazide (CA INDEX NAME)

Absolute stereochemistry.



RN 862462-63-3 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(2-methoxyethyl)-α-oxo- (CA INDEX NAME)

Absolute stereochemistry.



IT **380226-97-1P 785047-47-4P 862462-64-4P 862462-65-5P**
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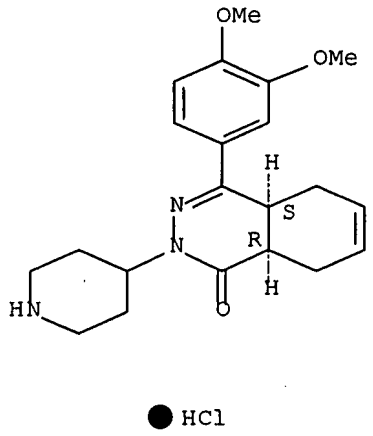
(preparation of phthalazinone derivs. as PDE4 inhibitors)
RN 380226-97-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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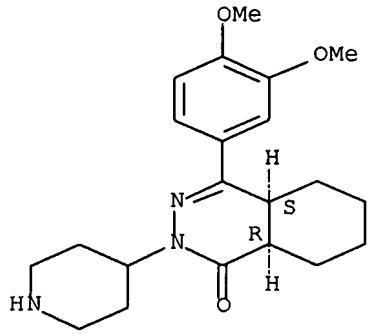
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2-(4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



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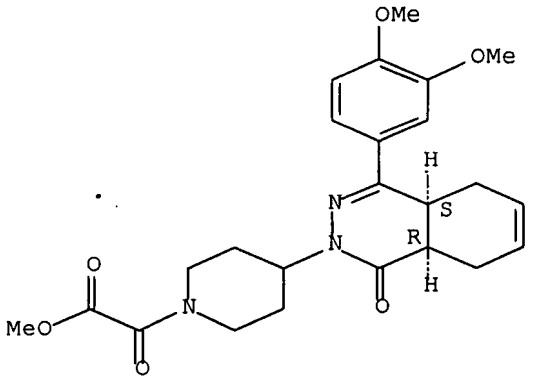
CN 1-Piperidineacetic acid, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-α-oxo-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



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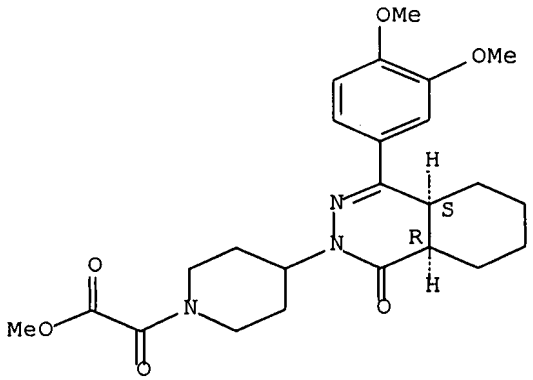
CN 1-Piperidineacetic acid, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-α-oxo-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07D401-04
ICS C07D401-14; A61K031-498; A61P011-00
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**, **63**
IT **862462-47-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of phthalazinone derivs. as PDE4 inhibitors)
IT **862462-48-4P 862462-50-8P 862462-51-9P**
862462-53-1P 862462-54-2P 862462-55-3P
862462-56-4P 862462-57-5P 862462-58-6P
862462-59-7P 862462-60-0P 862462-61-1P
862462-62-2P 862462-63-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phthalazinone derivs. as PDE4 inhibitors)
IT **380226-97-1P** 415927-59-2P **785047-47-4P**

862462-64-4P 862462-65-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phthalazinone derivs. as PDE4 inhibitors)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:232615 HCAPLUS Full-text
DOCUMENT NUMBER: 142:291403
TITLE: Use of phosphodiesterase 4 (PDE4) inhibitors for the treatment of diabetes mellitus
INVENTOR(S): Hauser, Daniela; Hanauer, Guido; Grundler, Gerhard; Schmidt, Beate; Kemkowski, Joerg; Kley, Hans-Peter
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2005023253	A1	20050317	WO 2004-EP52005		20040902	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW						
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG						
AU 2004269923	A2	20050317	AU 2004-269923		20040902	<--
AU 2004269923	A1	20050317				
CA 2537230	A1	20050317	CA 2004-2537230		20040902	<--
JP 2007504201	T	20070301	JP 2006-525146		20040902	<--
MX 2006PA02521	A	20060620	MX 2006-PA2521		20060303	<--
US 2006281745	A1	20061214	US 2006-570622		20060303	<--
PRIORITY APPLN. INFO.:			EP 2003-20126	A	20030905	<--
			WO 2004-EP52005	W	20040902	<--

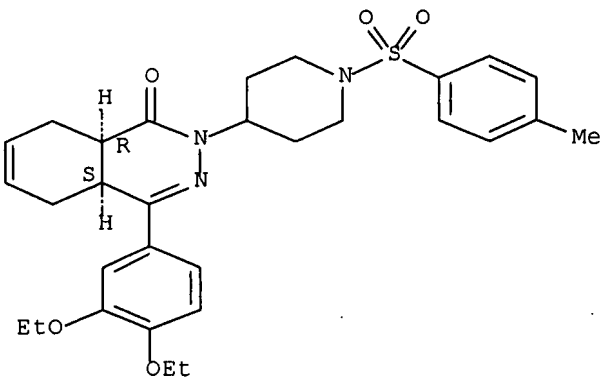
ED Entered STN: 17 Mar 2005
AB The invention discloses the use of certain known PDE4 inhibitors for the treatment of diabetes mellitus and accompanying disorders thereof.
IT **449760-14-9 449760-15-0 449760-16-1**
449760-17-2 449760-19-4 449760-20-7
449760-21-8 449760-22-9 449760-23-0
449760-24-1 449760-25-2 449760-26-3
449760-28-5 449760-29-6 449760-30-9
449760-35-4 449760-40-1 449760-42-3
449760-47-8 449760-48-9 449760-49-0
449760-50-3 449760-51-4 449760-52-5
449760-53-6 449760-56-9 449760-57-0
449760-58-1 596102-01-1 596102-07-7
596102-09-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphodiesterase 4 inhibitors for treatment of diabetes mellitus)

RN 449760-14-9 HCAPLUS

CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

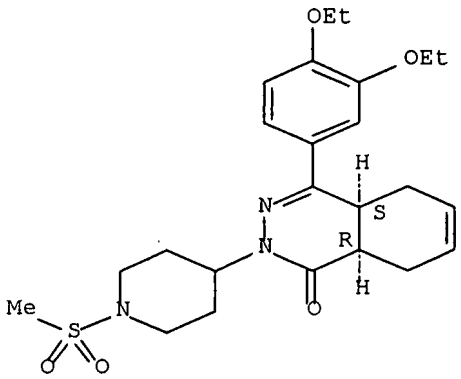
Absolute stereochemistry.



RN 449760-15-0 HCAPLUS

CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

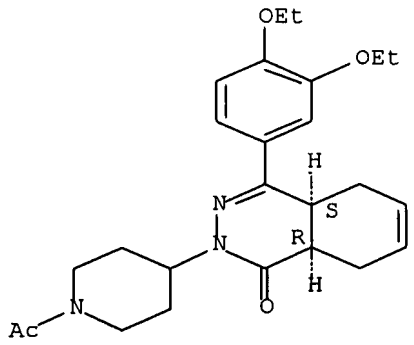
Absolute stereochemistry.



RN 449760-16-1 HCAPLUS

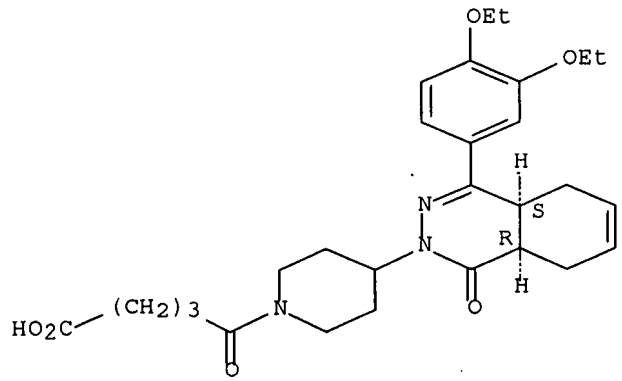
CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



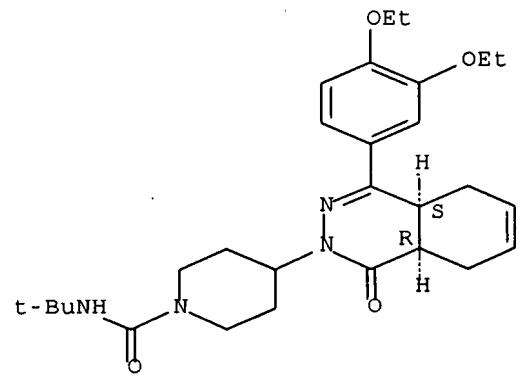
RN 449760-17-2 HCAPLUS
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



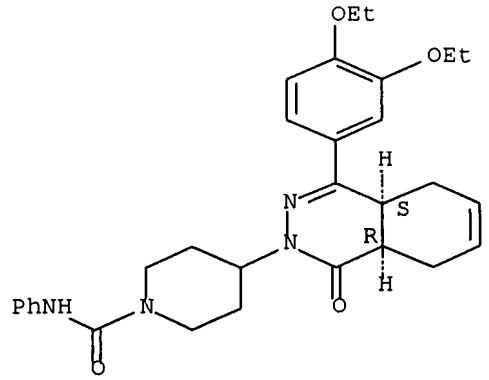
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



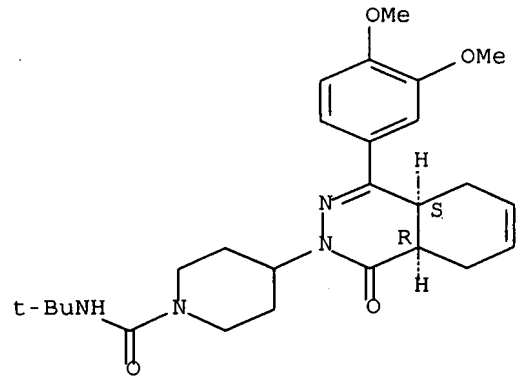
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



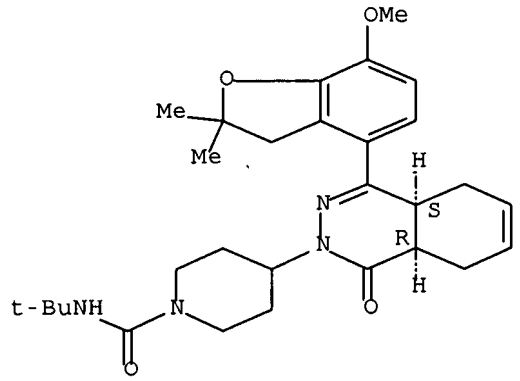
RN 449760-21-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

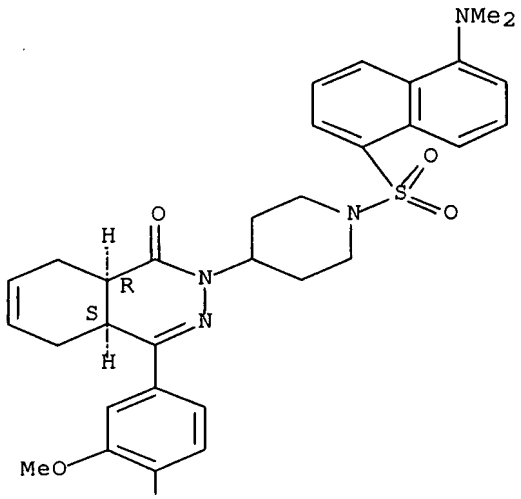
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

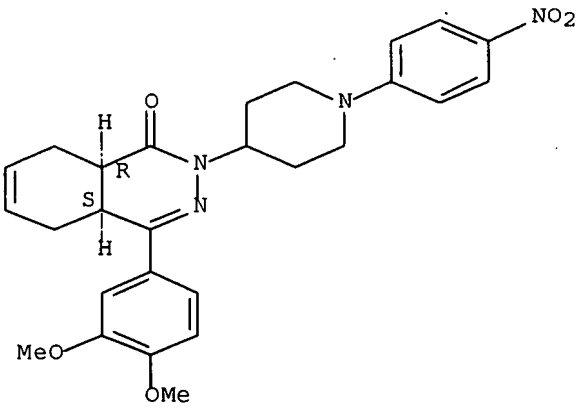


PAGE 2-A

OMe

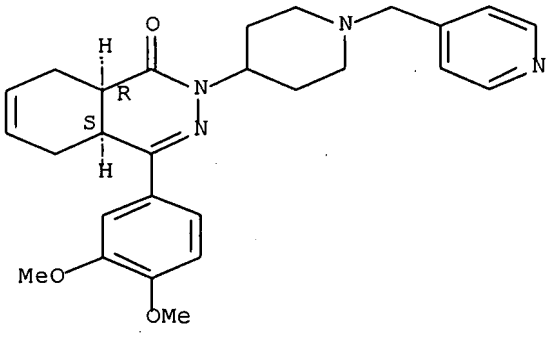
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



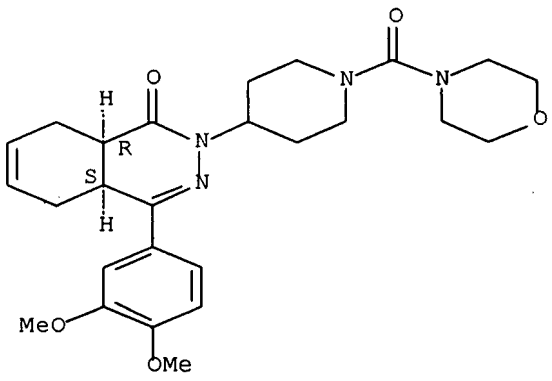
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



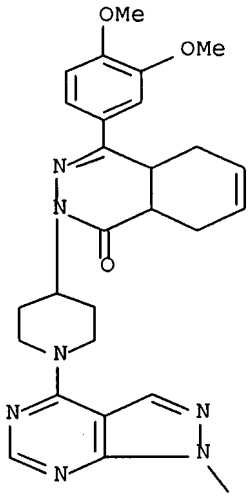
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A



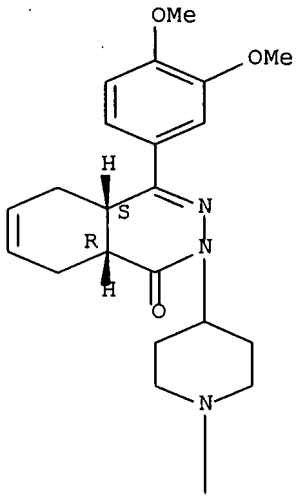
PAGE 2-A

Me

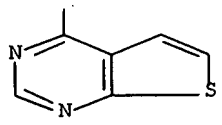
RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

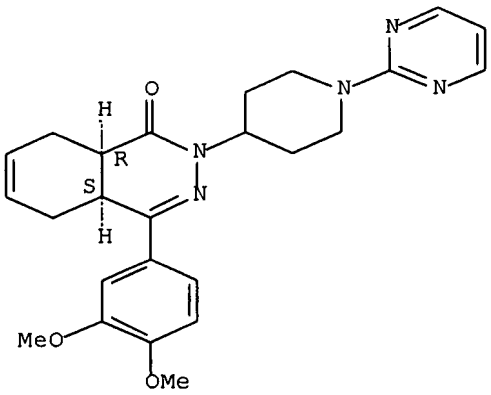


PAGE 2-A



RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

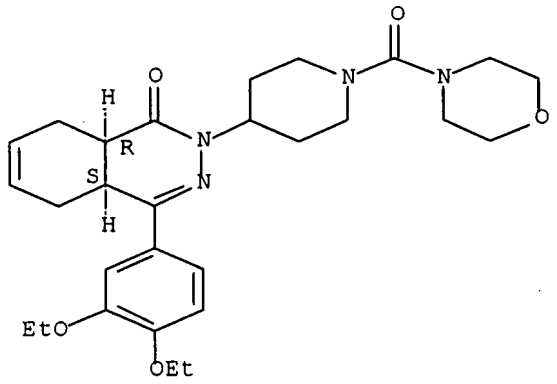
Absolute stereochemistry.



RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

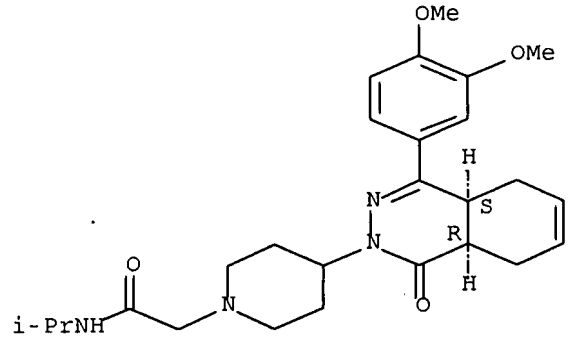
oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



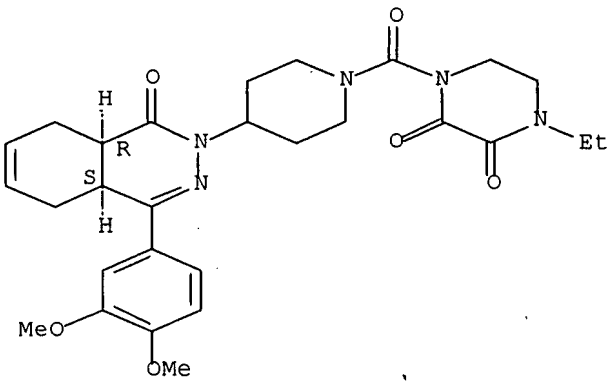
RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



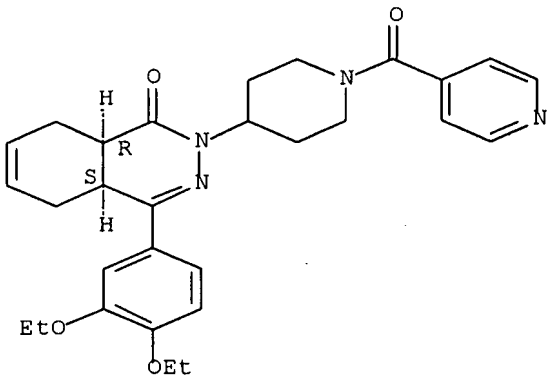
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



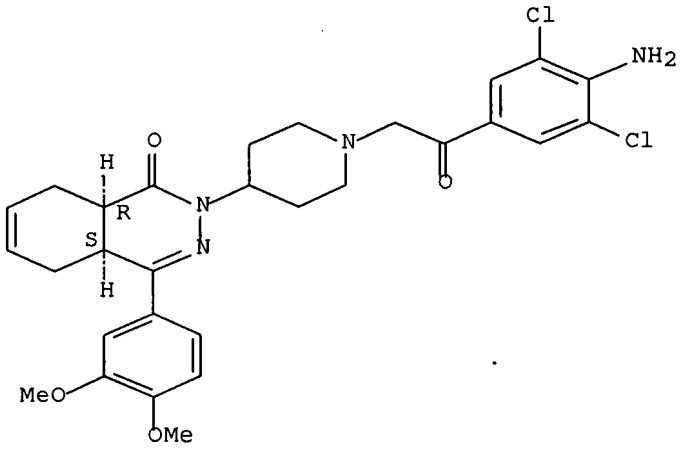
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



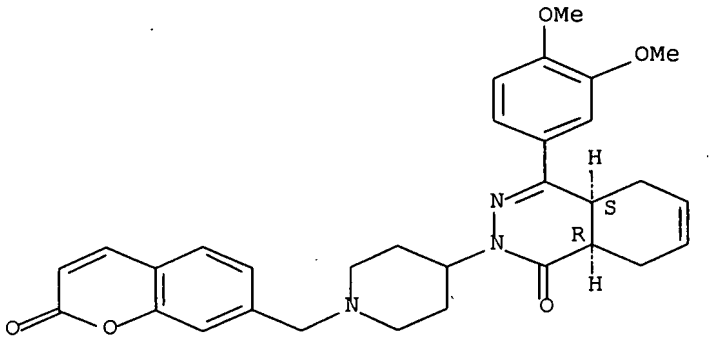
RN 449760-48-9 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



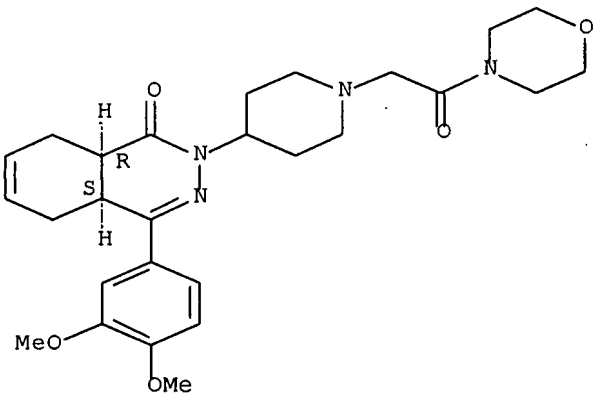
RN 449760-49-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



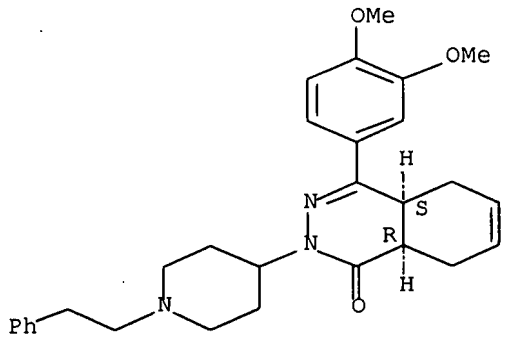
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



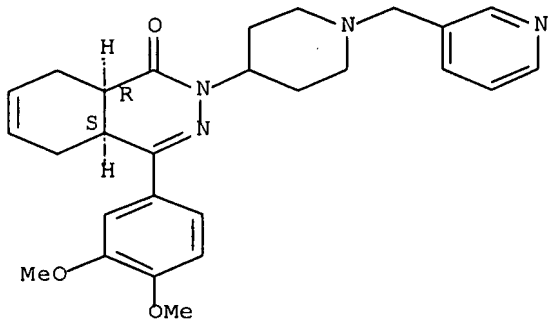
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



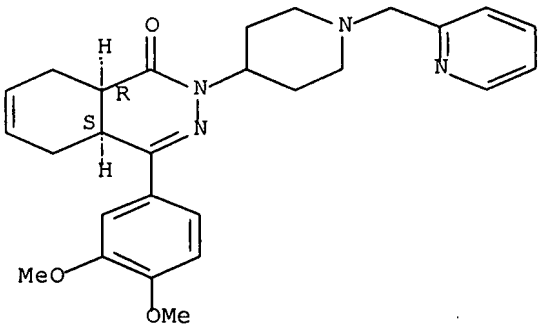
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



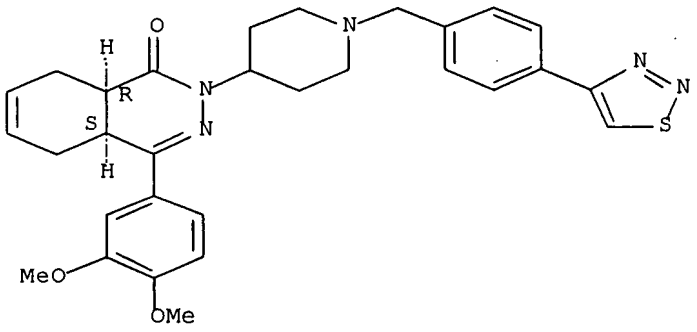
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



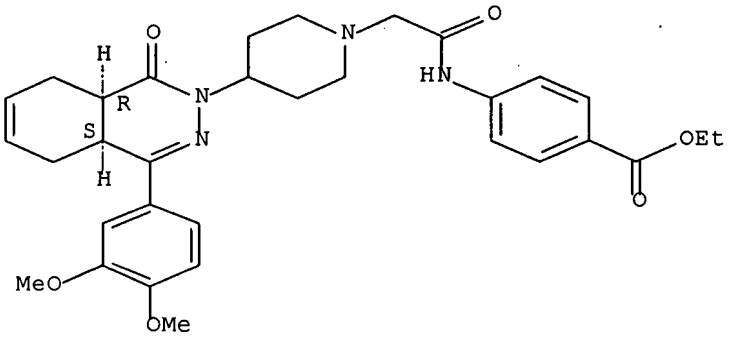
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



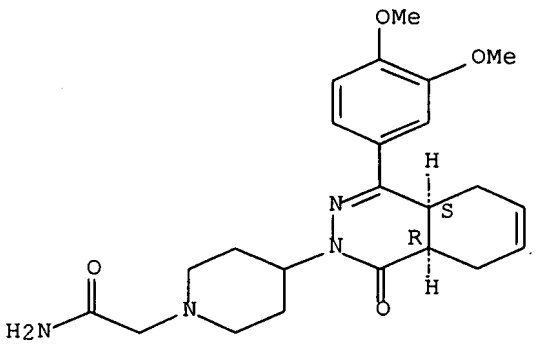
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

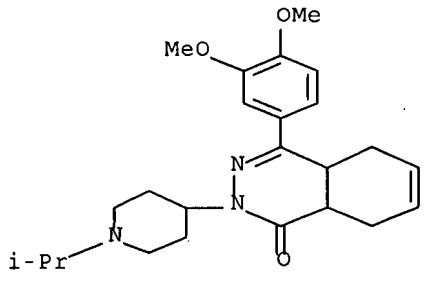


RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.

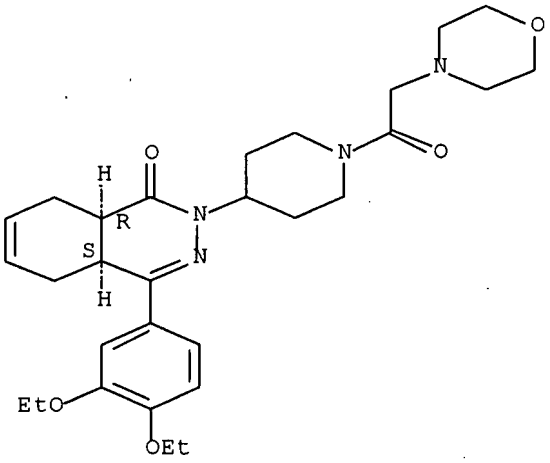


RN 596102-01-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methylethyl)-4-piperidinyl]- (CA INDEX NAME)



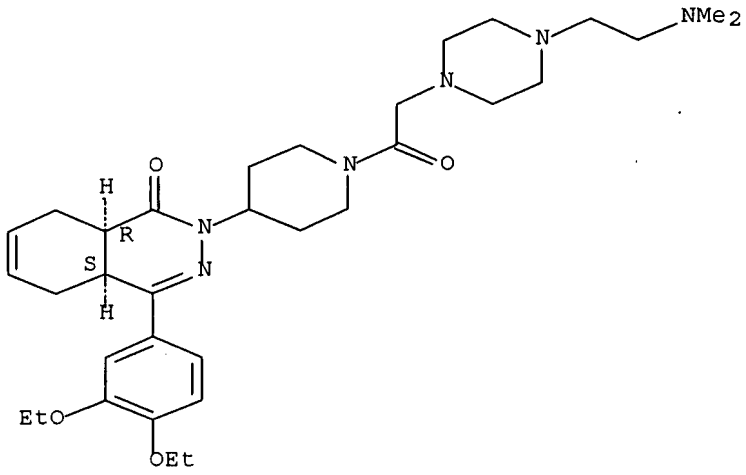
RN 596102-07-7 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-morpholinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596102-09-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[4-[2-(dimethylamino)ethyl]-1-piperazinyl]acetyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-435
ICS A61P003-10
CC 1-10 (**Pharmacology**)
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596102-09-9 847738-62-9 847908-94-5 847908-95-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 inhibitors for treatment of diabetes mellitus)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1036929 HCAPLUS Full-text
DOCUMENT NUMBER: 142:16825
TITLE: Composition comprising a PDE4 inhibitor and a PDE5 inhibitor
INVENTOR(S): Dunkern, Thorsten; Hatzelmann, Armin; Schudt, Christian; Grimminger, Friedrich; Ghofrani, Hossein Ardeschir
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004103407	A2	20041202	WO 2004-EP50869	20040519 <--
WO 2004103407	A3	20050217		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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CA 2525946	A1	20041202	CA 2004-2525946	20040519 <--
EP 1628682	A2	20060301	EP 2004-766017	20040519 <--
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BR 2004010326	A	20060523	BR 2004-10326	20040519 <--
CN 1791429	A	20060621	CN 2004-80013349	20040519 <--
JP 2006528229	T	20061214	JP 2006-530210	20040519 <--
MX 2005PA12302	A	20060130	MX 2005-PA12302	20051115 <--
US 2006094723	A1	20060504	US 2005-556888	20051115 <--

IN 2005MN01393	A	20070706	IN 2005-MN1393		20051213 <--
NO 2005005941	A	20051214	NO 2005-5941		20051214 <--
PRIORITY APPLN. INFO.:			EP 2003-11609	A	20030522 <--
			WO 2004-EP50869	W	20040519 <--

ED Entered STN: 03 Dec 2004

AB The invention relates to the combined administration of a PDE4 inhibitor and a PDE5 inhibitor for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or phosphodiesterase 5 (PDE5) activity is detrimental. Patients were administered orally one tablet of Roflumilase and once daily a tablet of Viagra. An example of another selected PDE4 inhibitor is I.

IT **449760-14-9 449760-15-0 449760-16-1**
449760-17-2 449760-19-4 449760-20-7
449760-21-8 449760-22-9 449760-23-0
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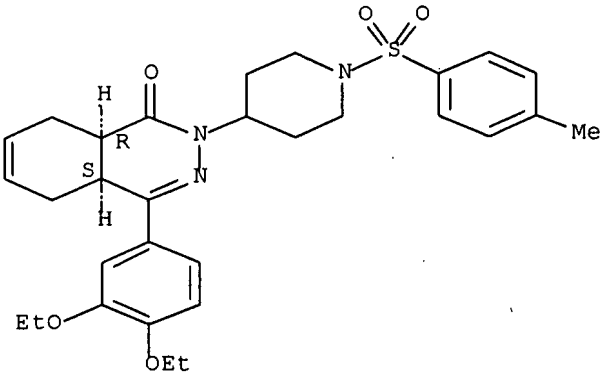
449760-53-6 449760-54-7 449760-55-8
449760-56-9 449760-57-0 449760-58-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a PDE4 inhibitor and a PDE5 inhibitor)

RN 449760-14-9 HCAPLUS

CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

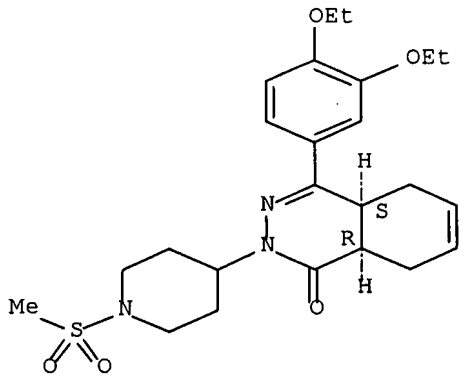
Absolute stereochemistry.



RN 449760-15-0 HCAPLUS

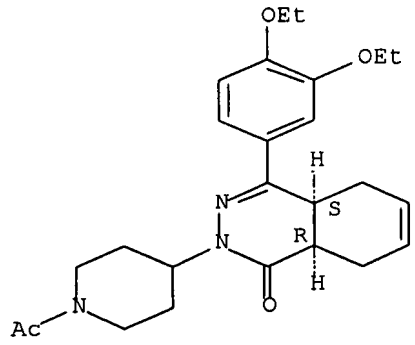
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



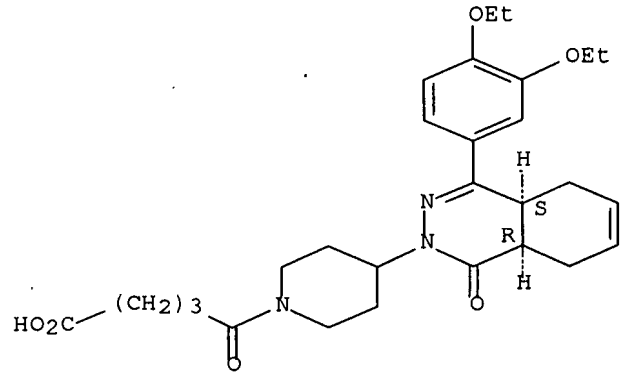
RN 449760-16-1 HCAPLUS
CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



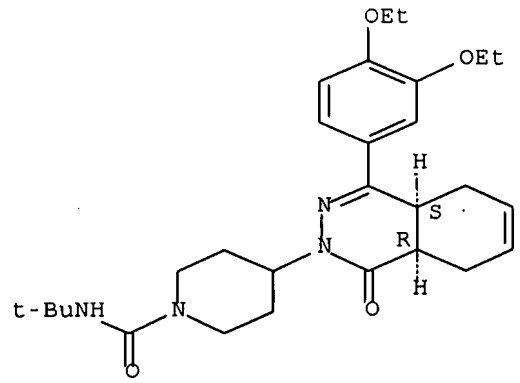
RN 449760-17-2 HCAPLUS
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



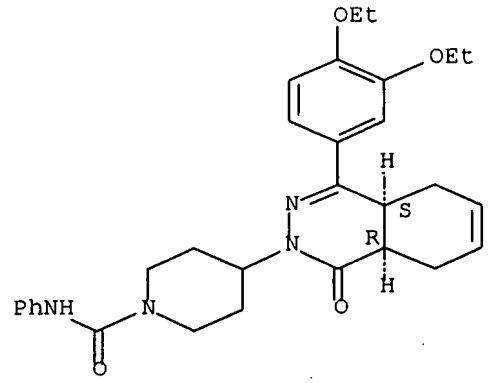
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



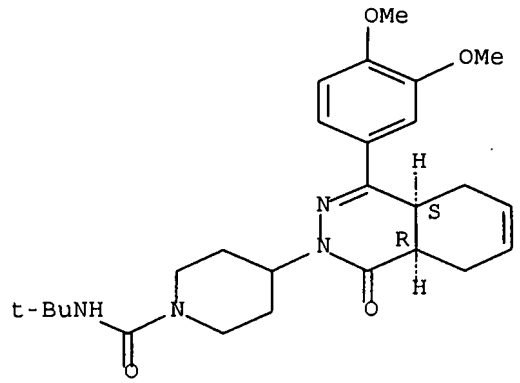
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



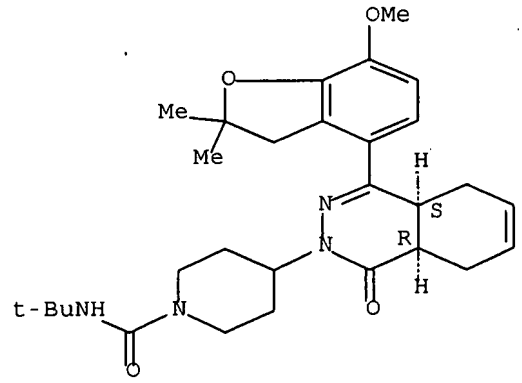
RN 449760-21-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

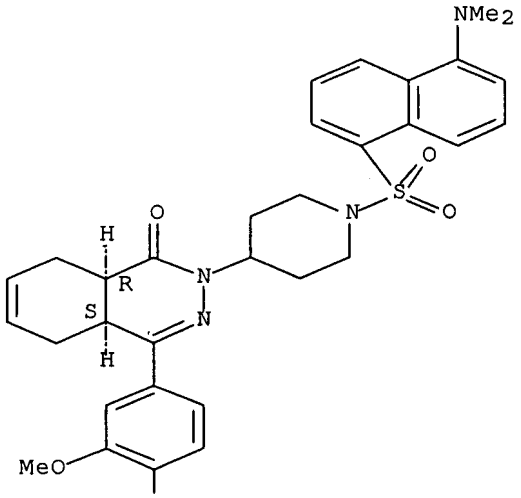
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

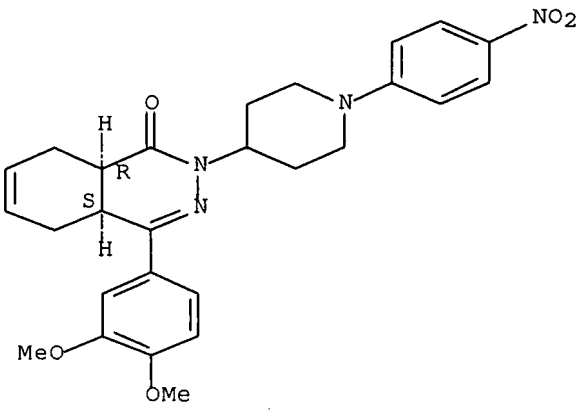


PAGE 2-A

OMe

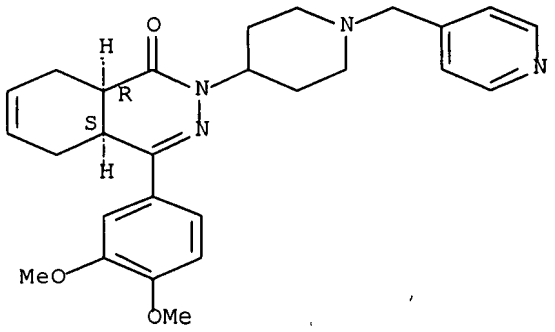
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



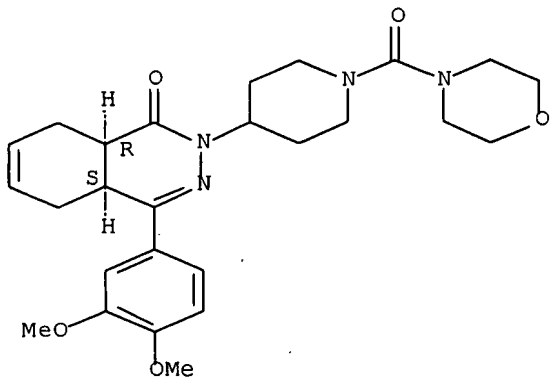
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



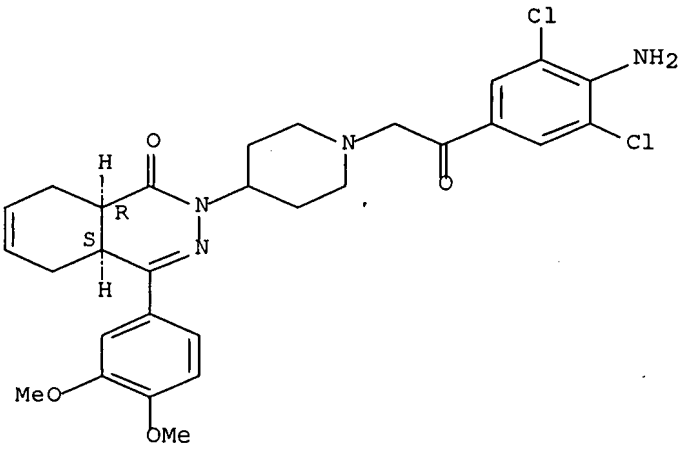
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



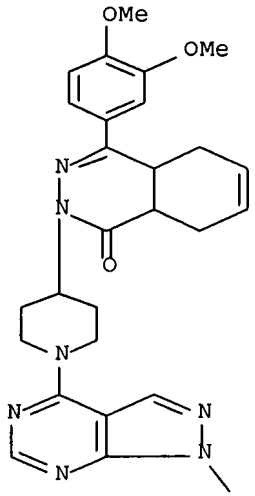
RN 449760-27-4 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A

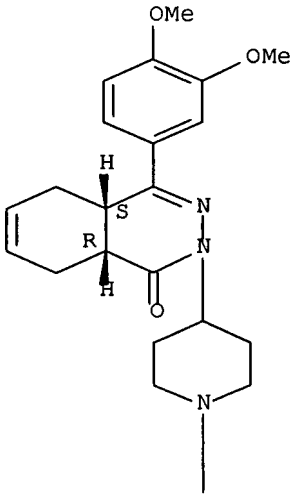


PAGE 2-A

RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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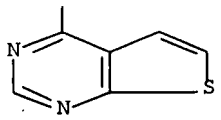
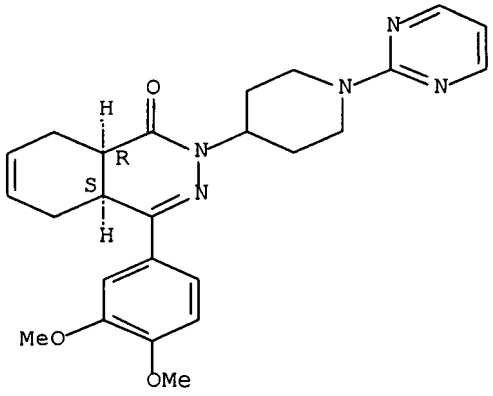


RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

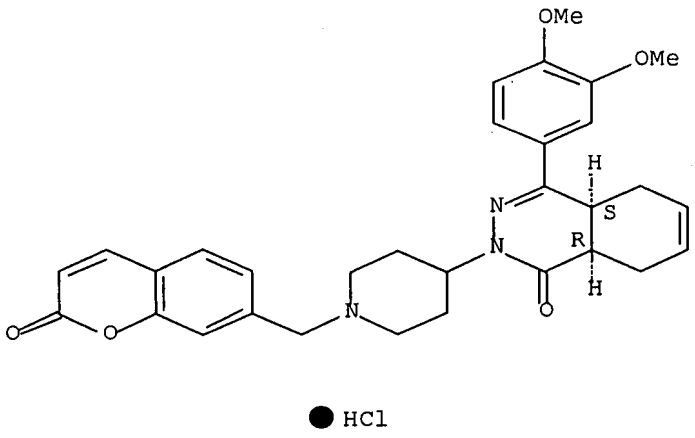
Absolute stereochemistry.



RN 449760-31-0 HCAPLUS

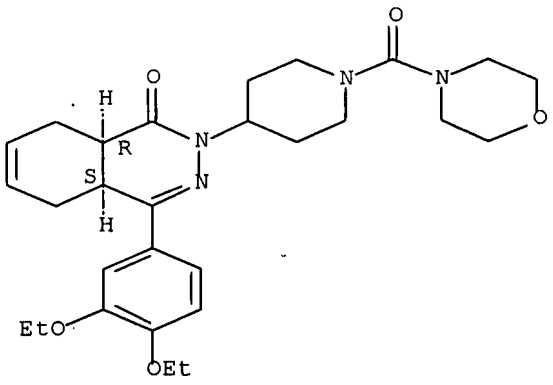
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



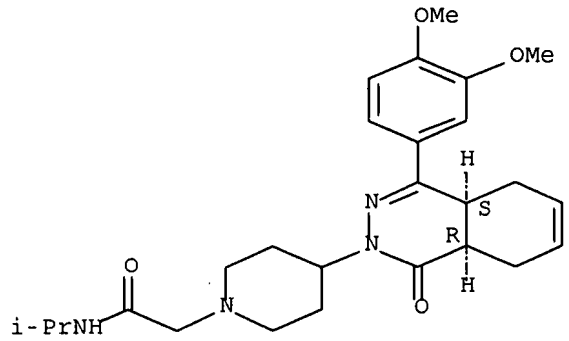
RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



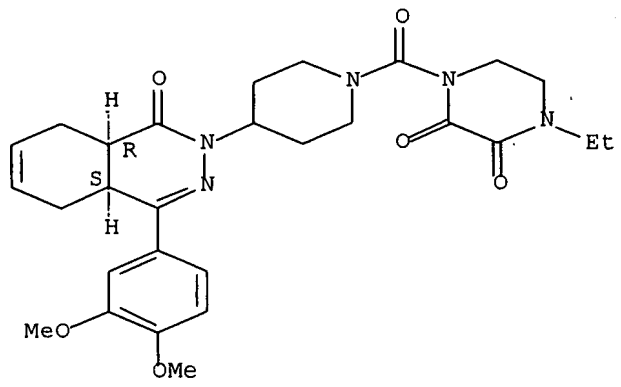
RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



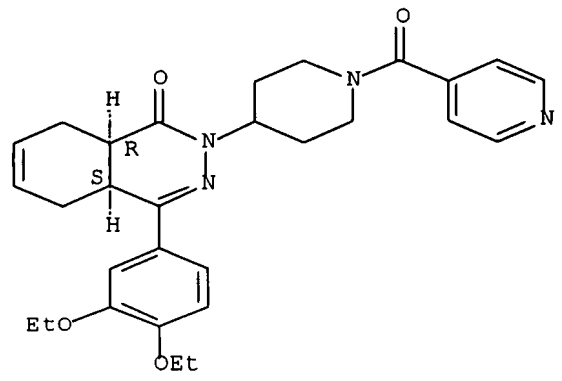
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



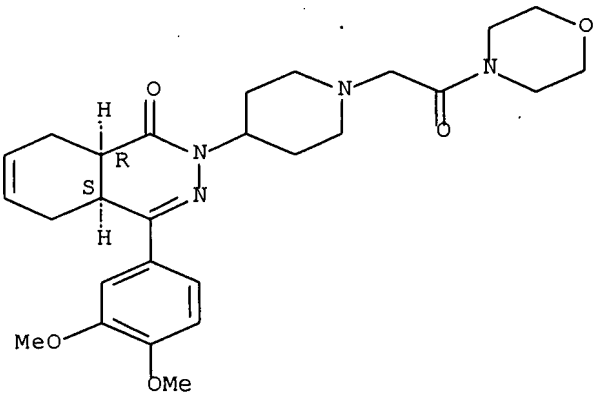
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



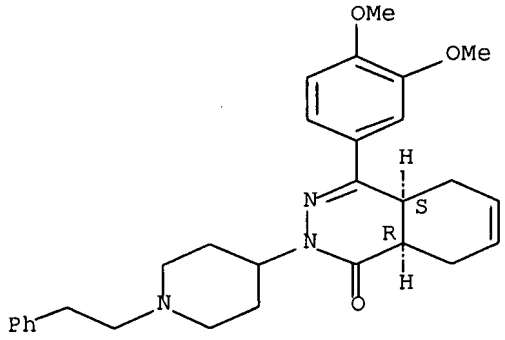
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



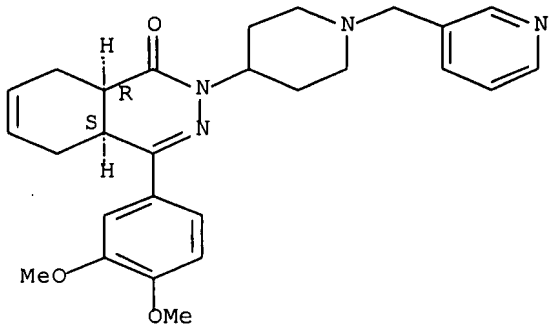
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



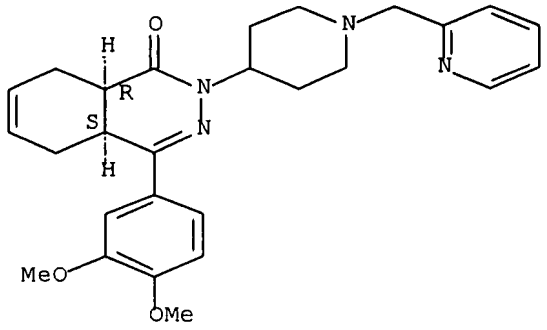
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



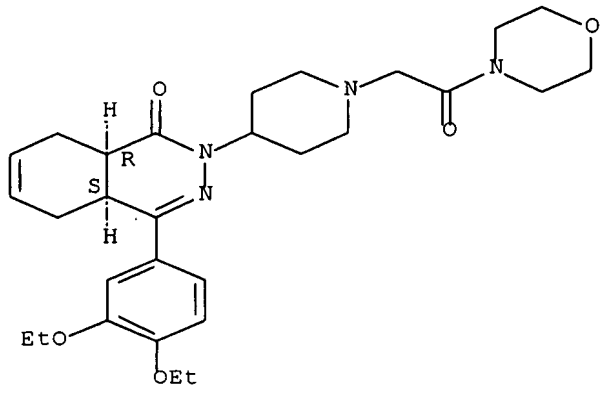
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



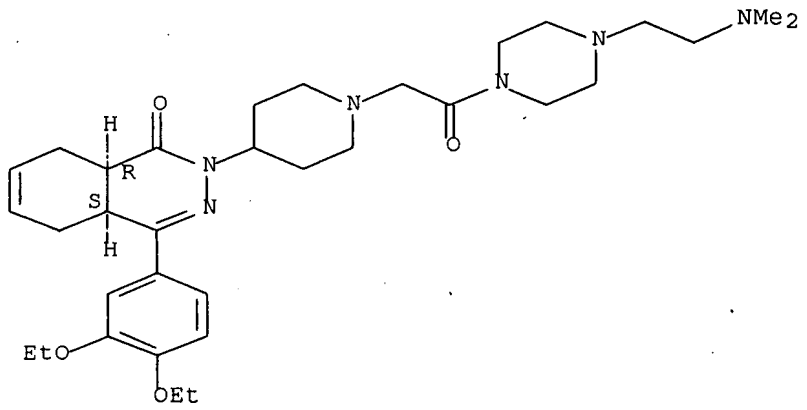
RN 449760-54-7 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



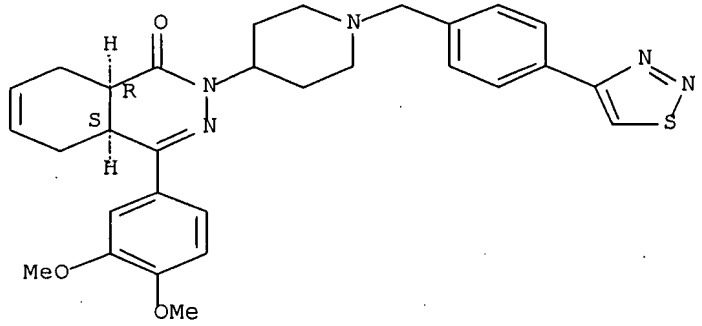
RN 449760-55-8 HCAPLUS
CN 1-Piperazineethanamine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



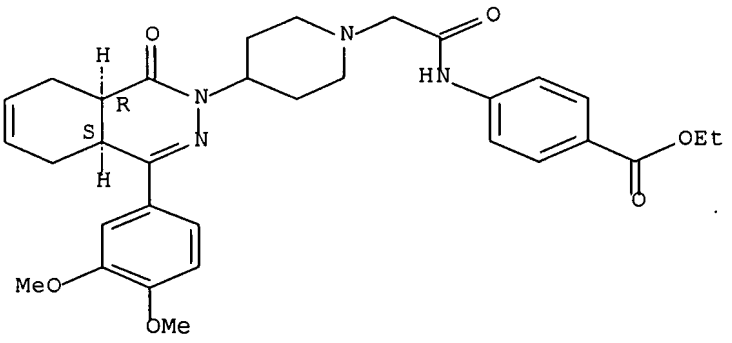
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



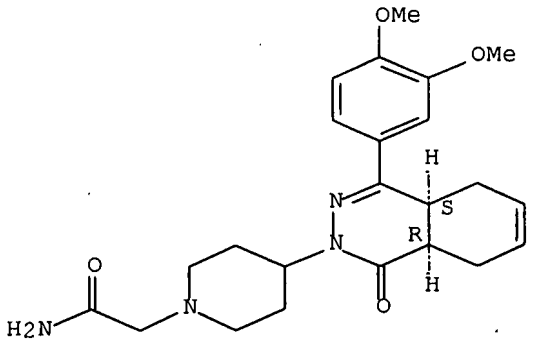
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K045-06
ICS A61K031-505; A61K031-44; A61K031-53; A61P009-04; A61P011-06; A61P013-12
CC 1-9 (**Pharmacology**)
Section cross-reference(s): **63**
IT 58-32-2, Dipyridamol 37762-06-4, Zaprinast 81840-15-5, Vesnarinone 106853-15-0 119409-07-3, SKF-96231 139755-83-2, Sildenafil 150452-18-9, ER 21355 153259-65-5, Cilomilast 158020-82-7, WIN 65579 162401-32-3, Roflumilast 167298-74-0, SCH-51866 170632-50-5, A 02131-1 171596-29-5, Tadalafil 178308-66-2, E-4010 184147-65-7, FR 181074 200803-37-8, CP-248 204077-66-7, KF-31327 212500-03-3, T-1032 215297-27-1, UK-343664 224157-99-7, SCH-59498 224785-90-4, Vardenafil 247568-68-9, FR-226807 247582-13-4, UK 371800 252231-60-0, BMS 263504 257892-33-4, AWD-12-281 268203-93-6, DA-8159 324572-93-2, T-0156
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449760-53-6 449760-54-7 449760-55-8
449760-56-9 449760-57-0 449760-58-1
548735-65-5, BF/GP-385 799841-02-4, FR 229934
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a PDE4 inhibitor and a PDE5 inhibitor)

L18 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:996001 HCAPLUS Full-text
DOCUMENT NUMBER: 141:406065
TITLE: Composition comprising a PDE-4 inhibitor and a TNF-alpha antagonist
INVENTOR(S): Barsig, Johannes; Weimar, Christian
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098633	A1	20041118	WO 2004-EP50748	20040510 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10581 A 20030512 <--
ED Entered STN: 19 Nov 2004
AB The invention relates to the combined administration of a PDE4 inhibitor and a TNFα antagonist selected from the group consisting of etanercept, onercept and pegsunercept for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNFα) activity is detrimental.
IT **449760-14-9 449760-15-0 449760-16-1**
449760-17-2 449760-19-4 449760-20-7
449760-21-8 449760-22-9 449760-23-0
449760-24-1 449760-25-2 449760-26-3
449760-28-5 449760-29-6 449760-30-9
449760-35-4 449760-40-1 449760-42-3
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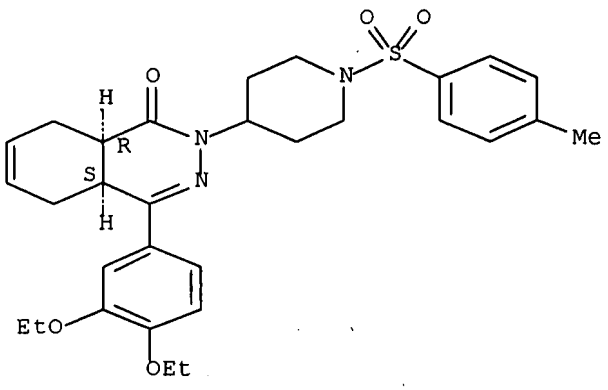
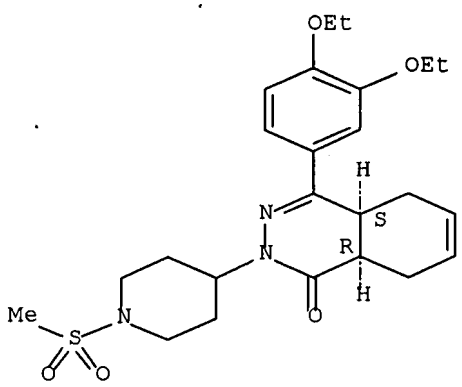
449760-50-3 449760-51-4 449760-52-5
449760-53-6 449760-54-7 449760-55-8
449760-56-9 449760-57-0 449760-58-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic activity of phosphodiesterase 4 inhibitors and TNFα antagonists)
RN 449760-14-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



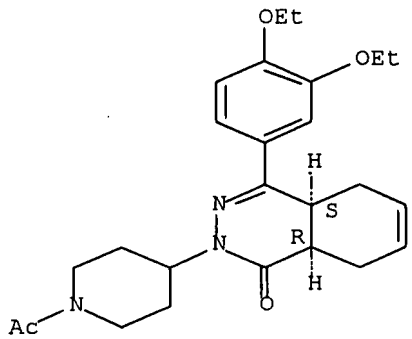
RN 449760-15-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



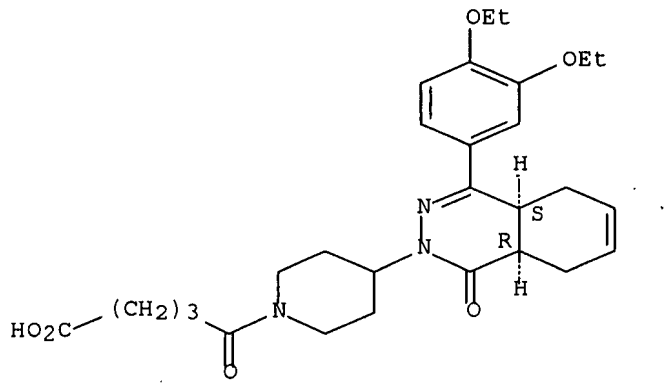
RN 449760-16-1 HCAPLUS
CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



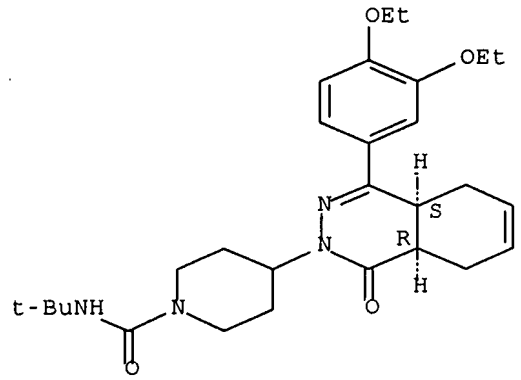
RN 449760-17-2 HCAPLUS
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



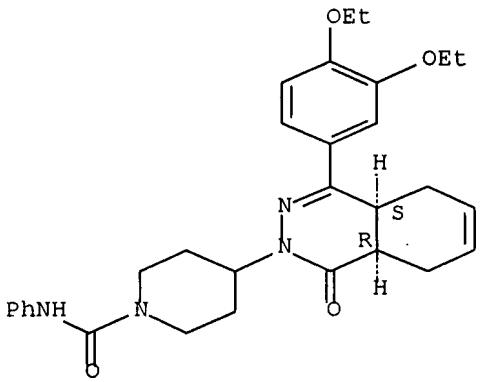
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



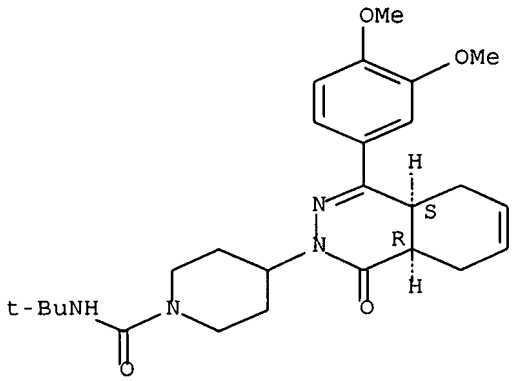
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



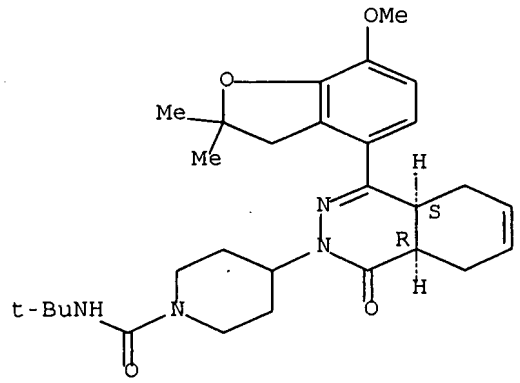
RN 449760-21-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

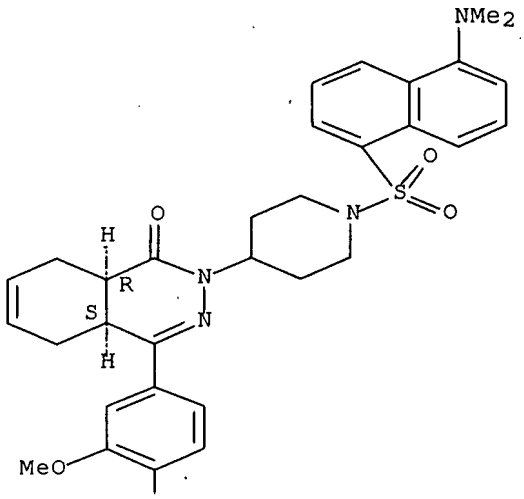
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

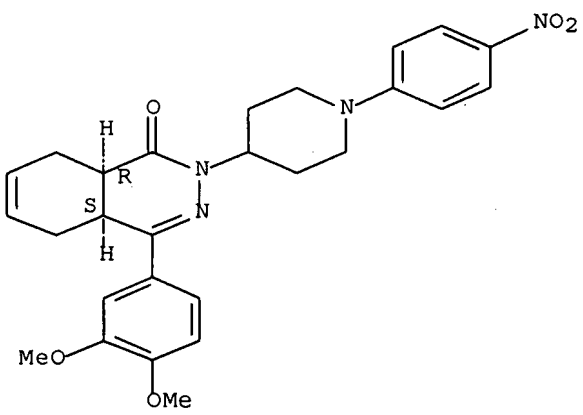
PAGE 1-A



PAGE 2-A

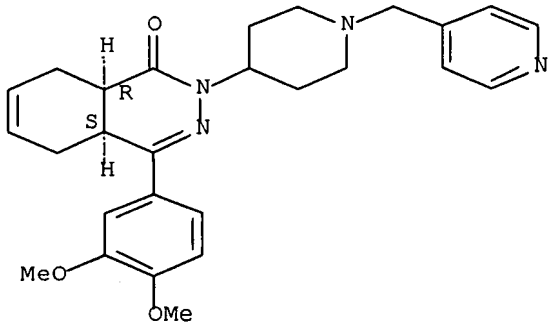
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



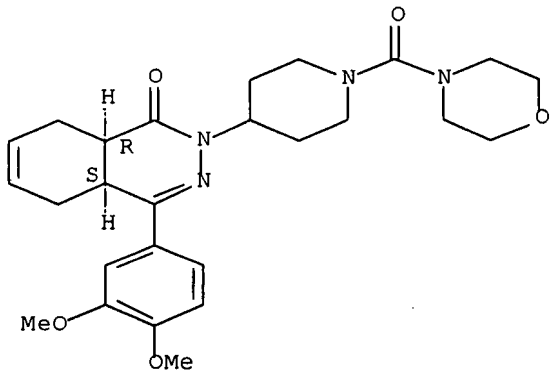
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



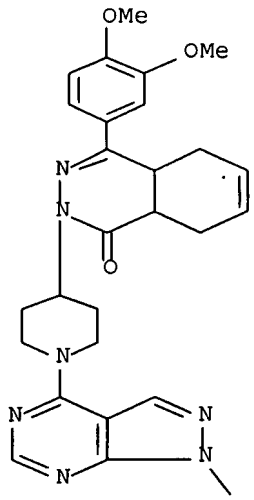
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A

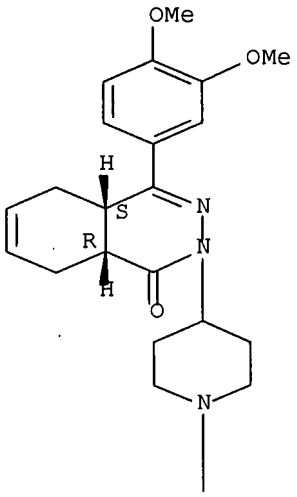


PAGE 2-A

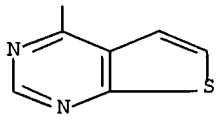
RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

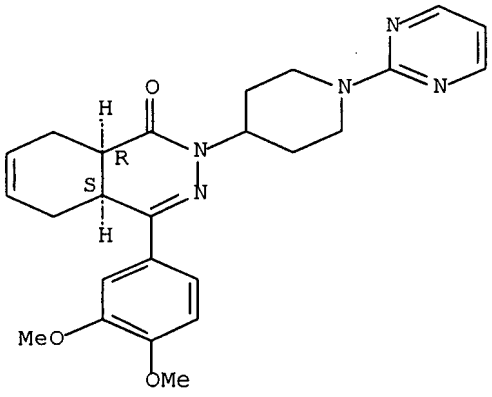


PAGE 2-A



RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

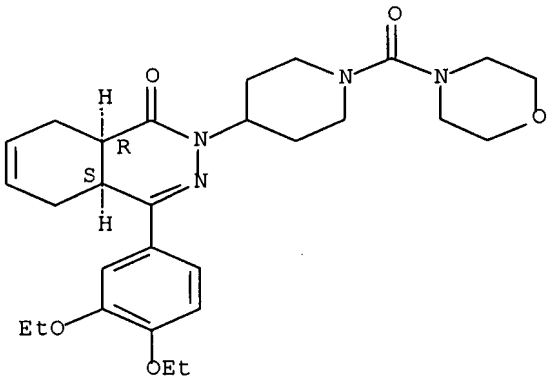
Absolute stereochemistry.



RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

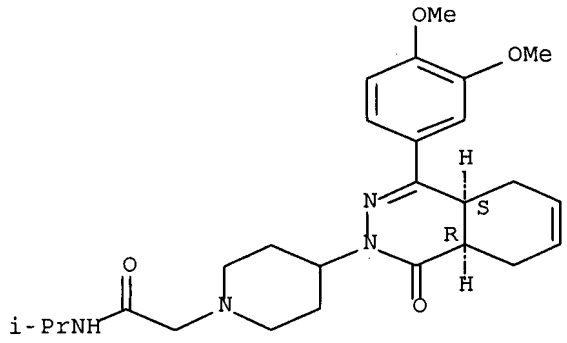
oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



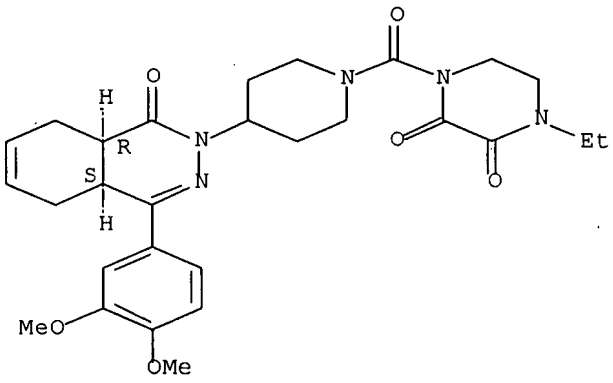
RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



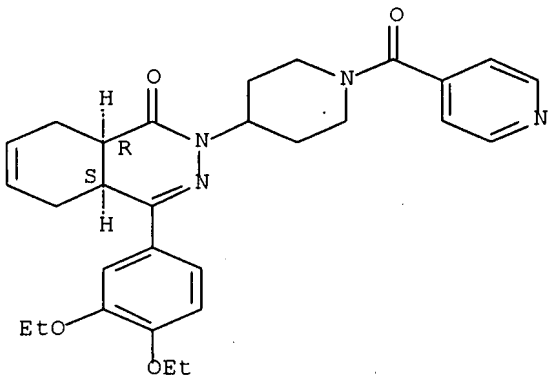
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



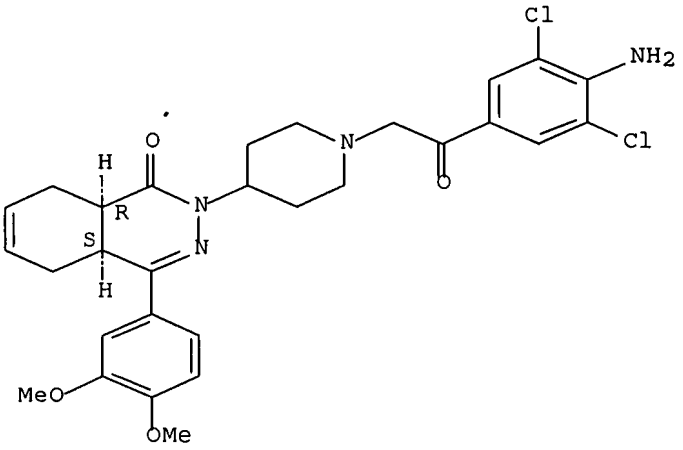
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



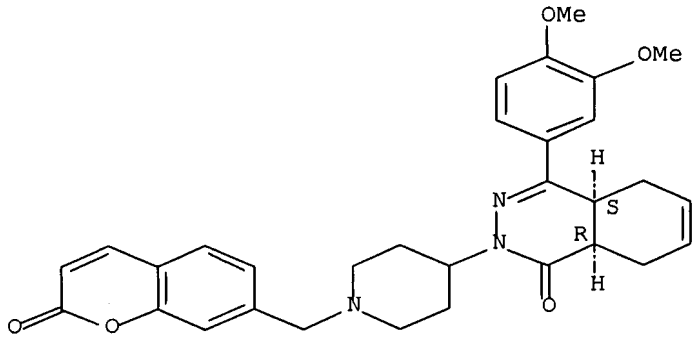
RN 449760-48-9 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



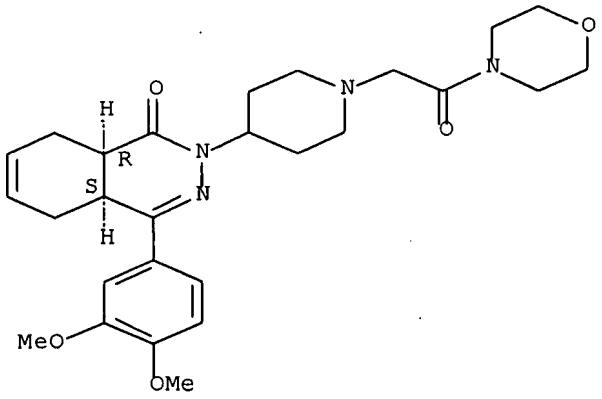
RN 449760-49-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



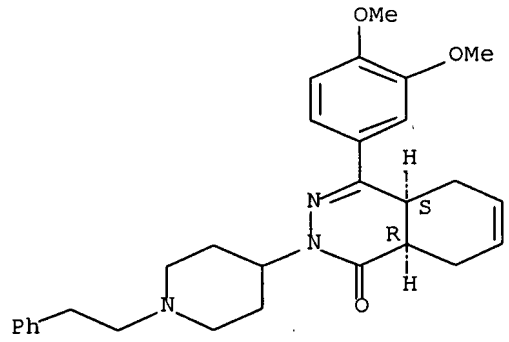
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



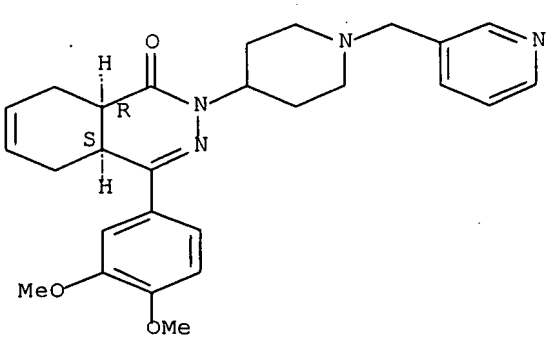
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



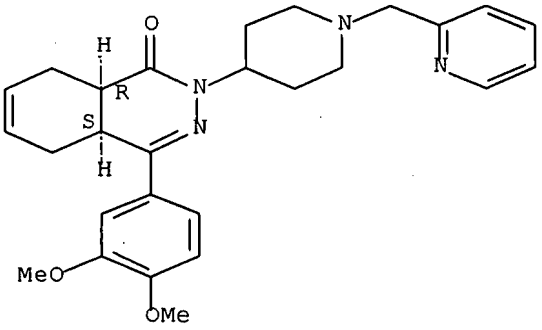
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



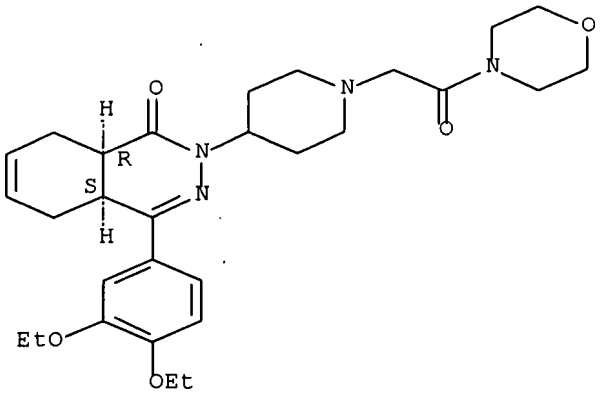
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



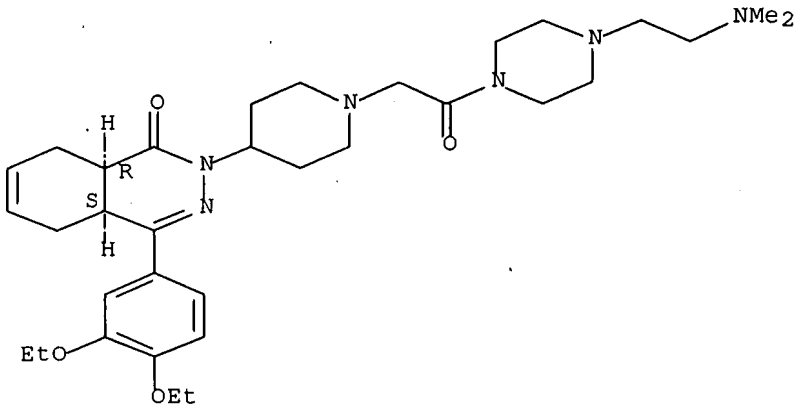
RN 449760-54-7 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



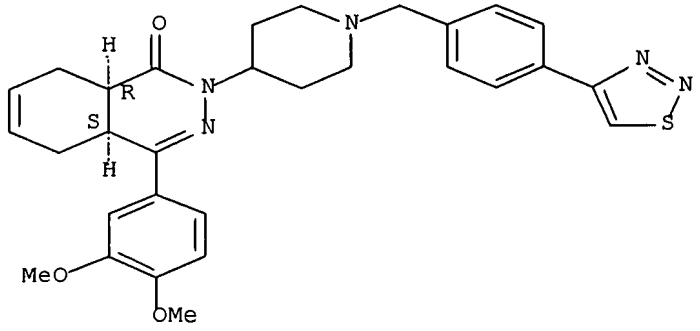
RN 449760-55-8 HCAPLUS
CN 1-Piperazineethanamine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



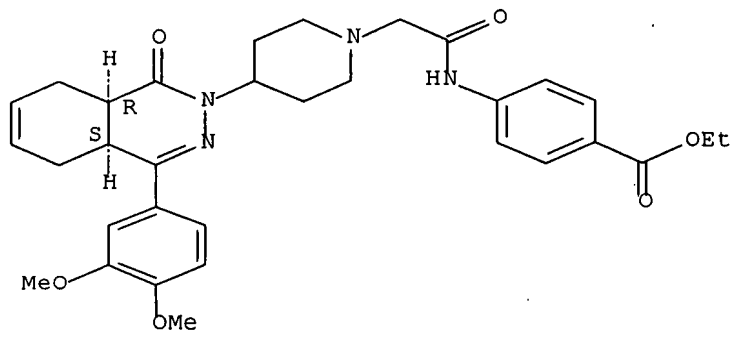
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



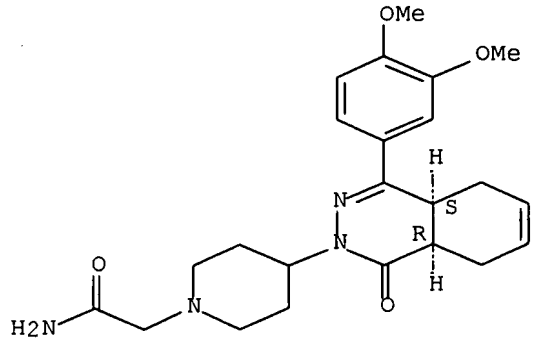
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K038-19
ICS A61K031-277; A61K031-502; A61P043-00
CC 1-7 (**Pharmacology**)
Section cross-reference(s): 15
IT 153259-65-5, Cilomilast 185243-69-0, Etanercept 199685-57-9, Onercept 257892-33-4, AWD 12-281 330988-75-5, Pegsunercept **449760-14-9** **449760-15-0** **449760-16-1** **449760-17-2** **449760-19-4** **449760-20-7** **449760-21-8** **449760-22-9** **449760-23-0** **449760-24-1** **449760-25-2** **449760-26-3** **449760-28-5** **449760-29-6** **449760-30-9** **449760-35-4** **449760-40-1** **449760-42-3** **449760-47-8** **449760-48-9** **449760-49-0** **449760-50-3** **449760-51-4** **449760-52-5** **449760-53-6** **449760-54-7** **449760-55-8** **449760-56-9** **449760-57-0** **449760-58-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic activity of phosphodiesterase 4 inhibitors and TNFα antagonists)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:995979 HCAPLUS Full-text
DOCUMENT NUMBER: 141:406064
TITLE: Composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy
INVENTOR(S): Barsig, Johannes
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

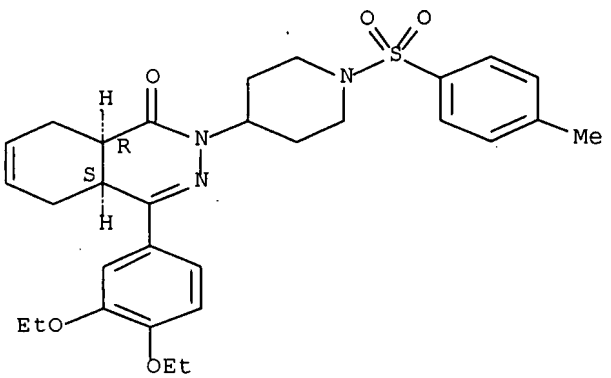
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098606	A1	20041118	WO 2004-EP50749	20040510 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10596 A 20030512 <--
ED Entered STN: 19 Nov 2004
AB The invention relates to the combined administration of a PDE4 inhibitor and shuIL-1R II for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental.
IT **449760-14-9 449760-15-0 449760-16-1**
449760-17-2 449760-19-4 449760-20-7
449760-21-8 449760-22-9 449760-23-0
449760-24-1 449760-25-2 449760-26-3
449760-28-5 449760-29-6 449760-30-9
449760-35-4 449760-40-1 449760-42-3
449760-47-8 449760-48-9 449760-49-0
449760-50-3 449760-51-4 449760-52-5
449760-53-6 449760-54-7 449760-55-8
449760-56-9 449760-57-0 449760-58-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy)
RN 449760-14-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

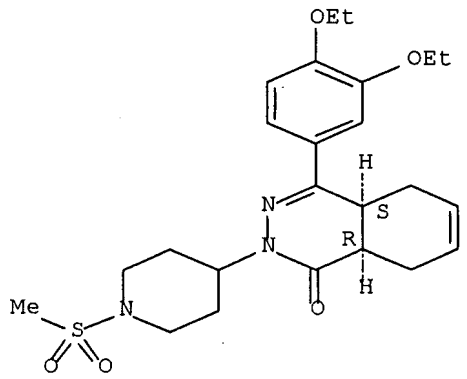
Absolute stereochemistry.



RN 449760-15-0 HCAPLUS

CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

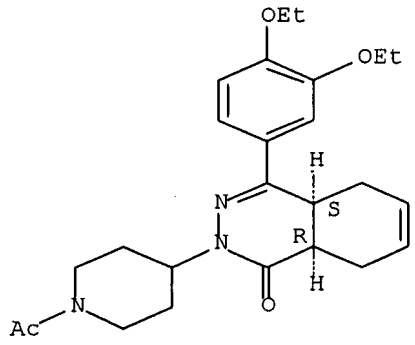
Absolute stereochemistry.



RN 449760-16-1 HCAPLUS

CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

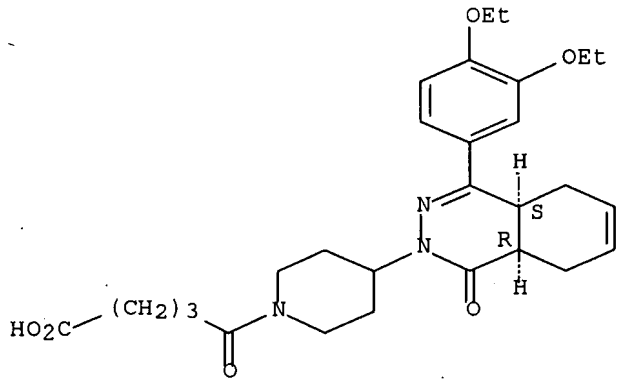
Absolute stereochemistry.



RN 449760-17-2 HCAPLUS

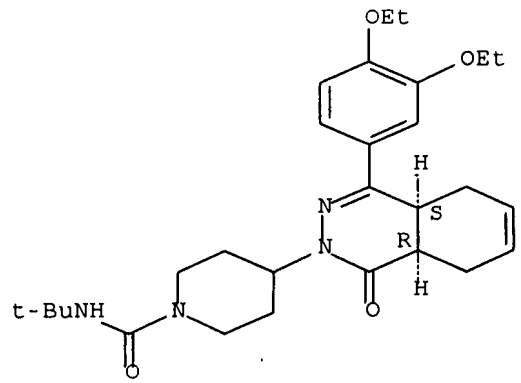
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



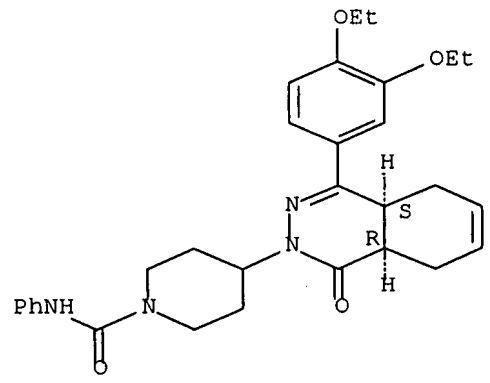
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



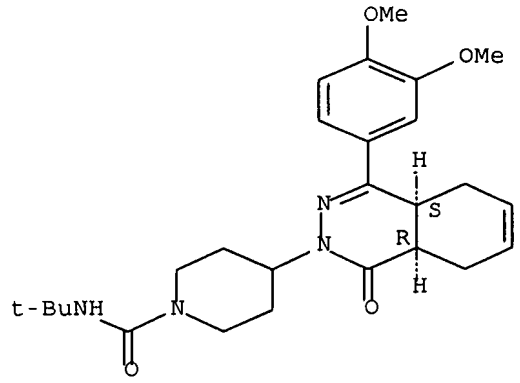
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



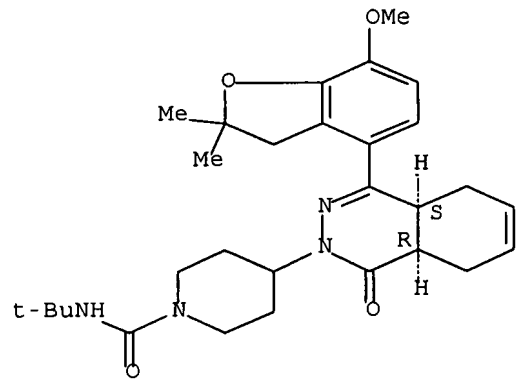
RN 449760-21-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

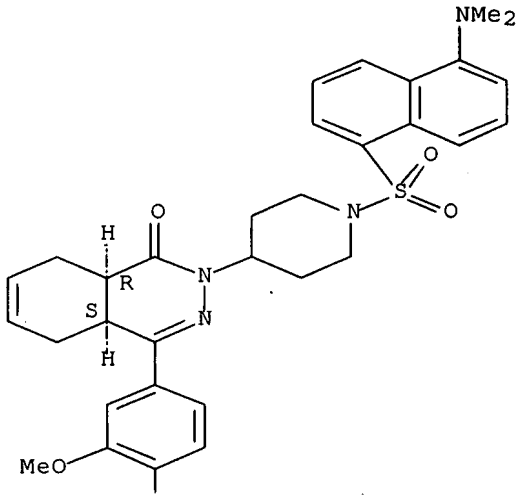
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

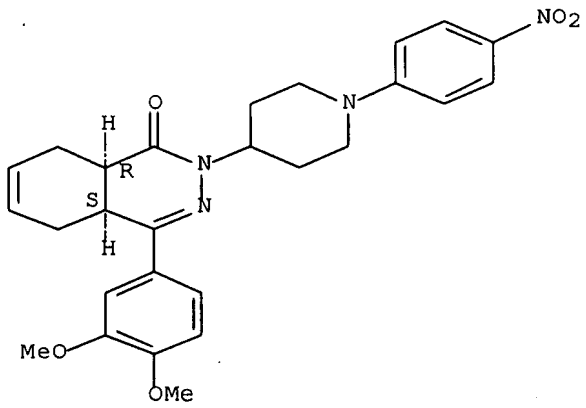


PAGE 2-A

OMe

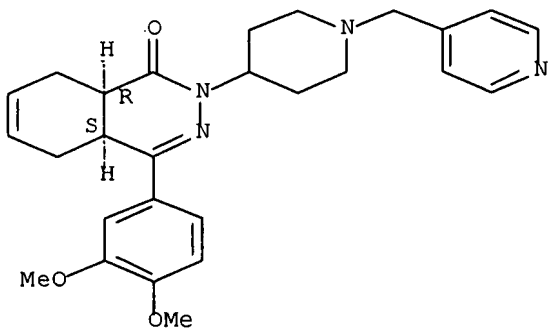
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



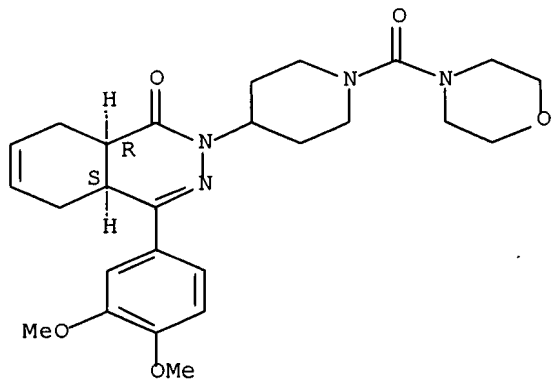
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



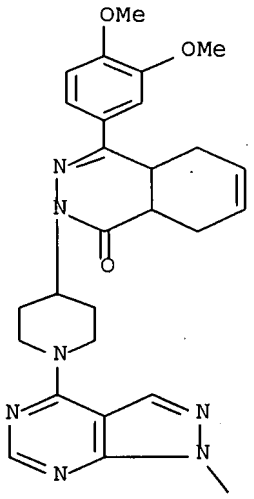
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A



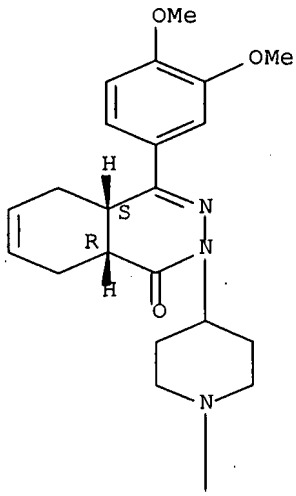
PAGE 2-A

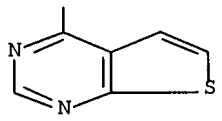
Me

RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

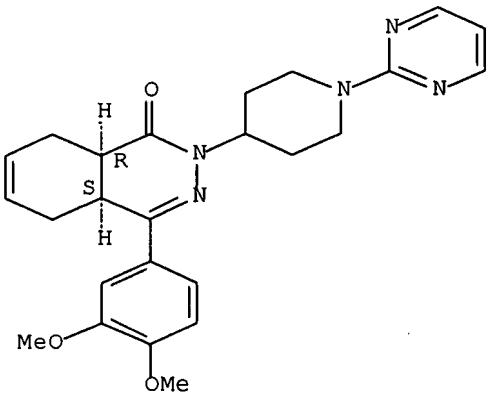
PAGE 1-A





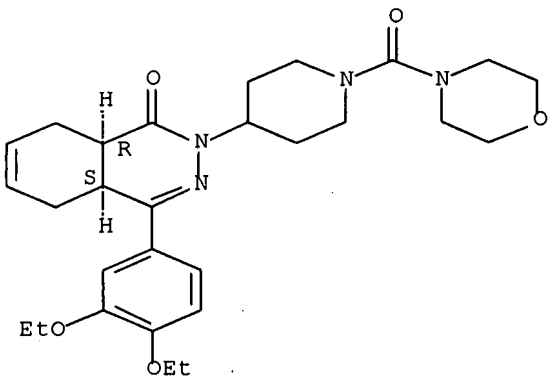
RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

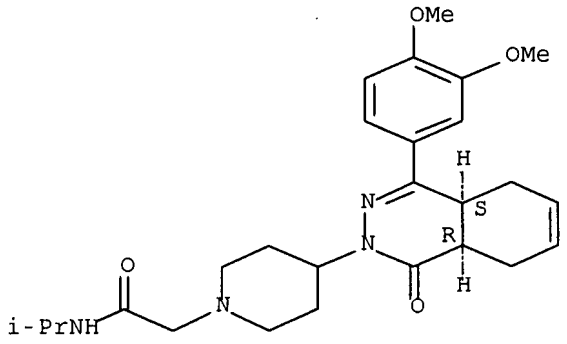
Absolute stereochemistry.



RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-

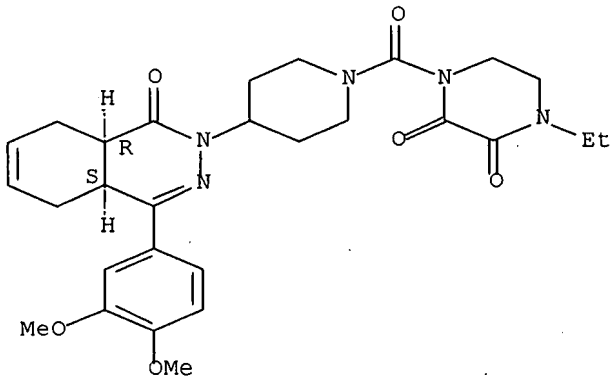
tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



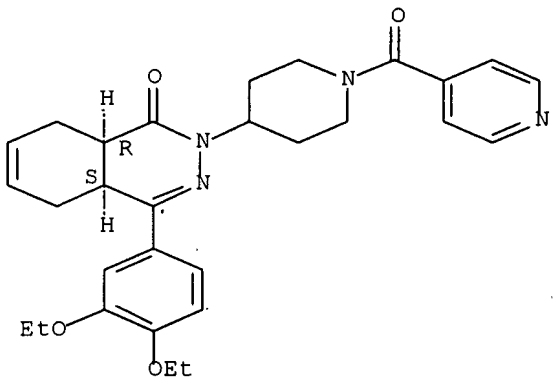
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



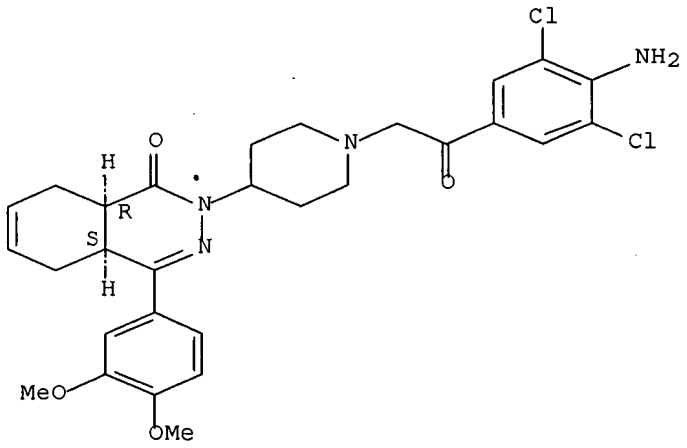
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



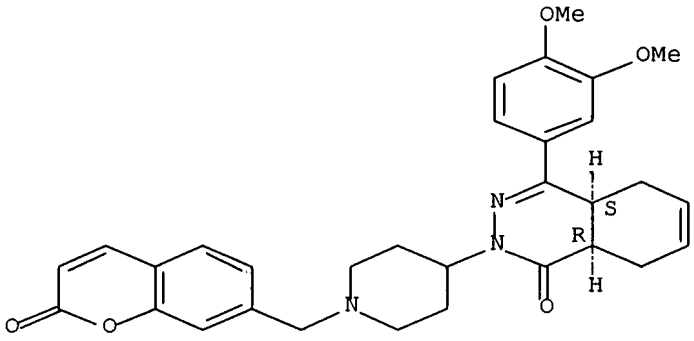
RN 449760-48-9 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(CA INDEX NAME)

Absolute stereochemistry.



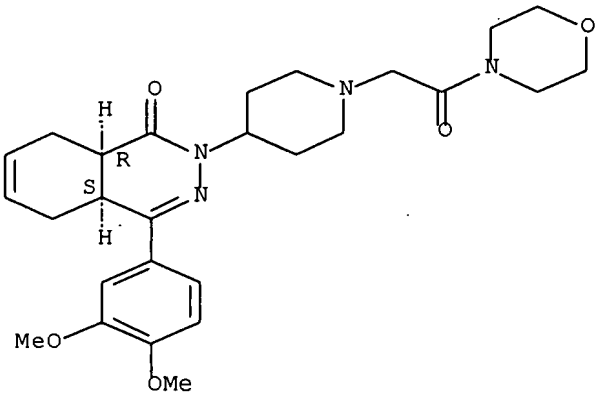
RN 449760-49-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



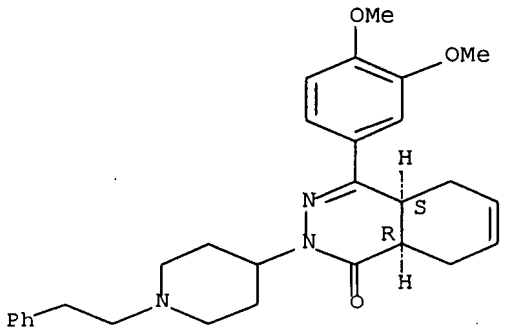
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



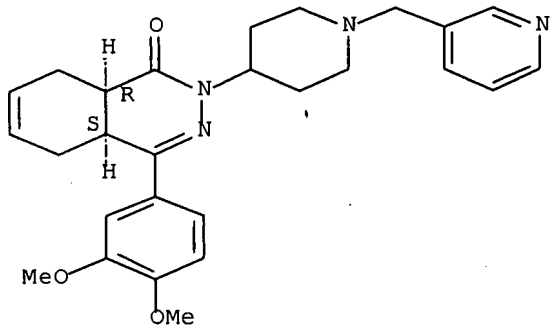
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



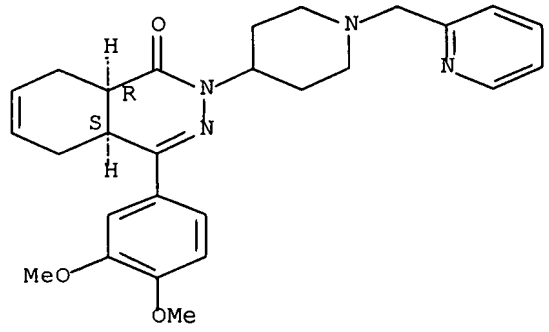
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



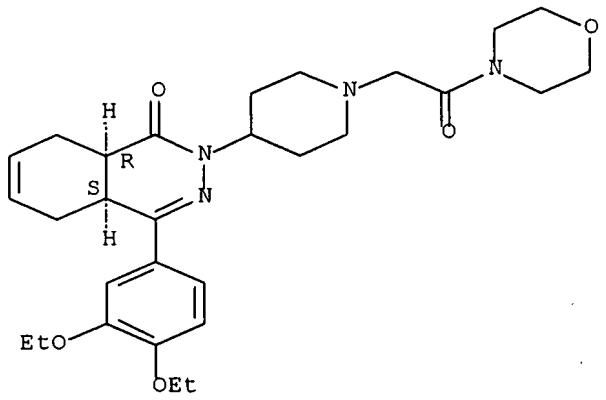
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



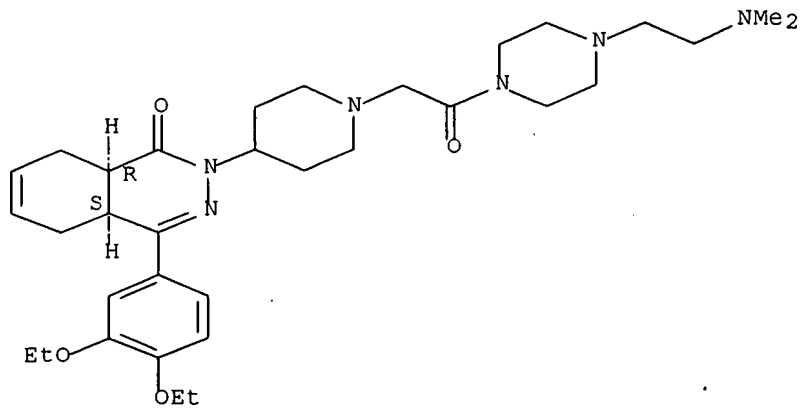
RN 449760-54-7 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



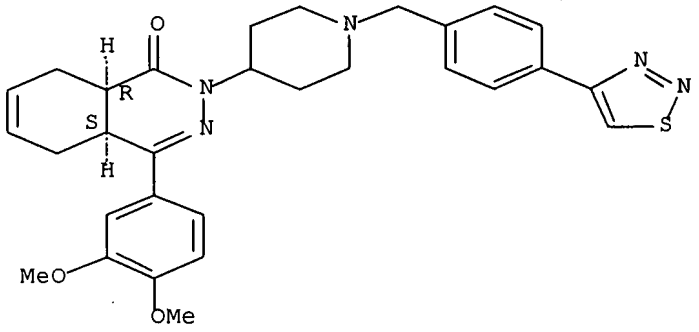
RN 449760-55-8 HCAPLUS
CN 1-Piperazineethanamine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



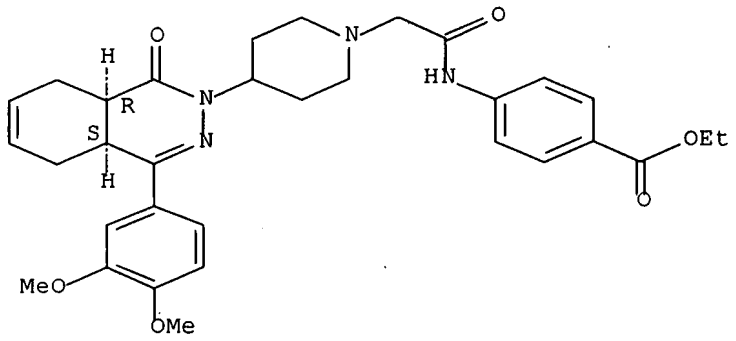
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



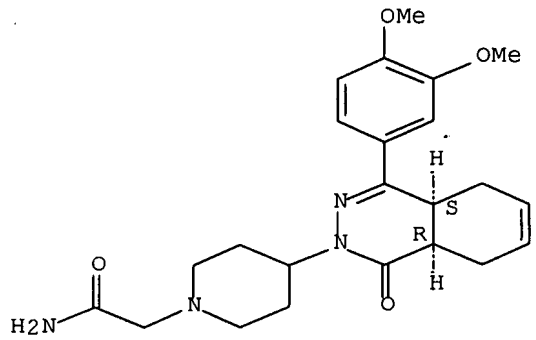
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-502
ICS A61K031-277; A61K038-17; A61K045-06; A61K031-4439; A61P029-00; A61P019-02; A61P017-06
CC 1-7 (**Pharmacology**)
IT 153259-65-5, Cilomilast 257892-33-4, AWD 12-281 **449760-14-9**
449760-15-0 449760-16-1 449760-17-2
449760-19-4 449760-20-7 449760-21-8
449760-22-9 449760-23-0 449760-24-1
449760-25-2 449760-26-3 449760-28-5
449760-29-6 449760-30-9 449760-35-4
449760-40-1 449760-42-3 449760-47-8
449760-48-9 449760-49-0 449760-50-3
449760-51-4 449760-52-5 449760-53-6
449760-54-7 449760-55-8 449760-56-9
449760-57-0 449760-58-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:995978 HCAPLUS Full-text
DOCUMENT NUMBER: 141:406063
TITLE: Pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for treatment of disease
INVENTOR(S): Barsig, Johannes
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098605	A1	20041118	WO 2004-EP50747	20040510 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10631 A 20030512 <--
ED Entered STN: 19 Nov 2004
AB The invention relates to the combined administration of a PDE4 inhibitor and IL-1 Trap for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental.
IT **449760-14-9 449760-15-0 449760-16-1**
449760-17-2 449760-19-4 449760-20-7
449760-21-8 449760-22-9 449760-23-0
449760-24-1 449760-25-2 449760-26-3
449760-28-5 449760-29-6 449760-30-9

449760-35-4 449760-40-1 449760-42-3
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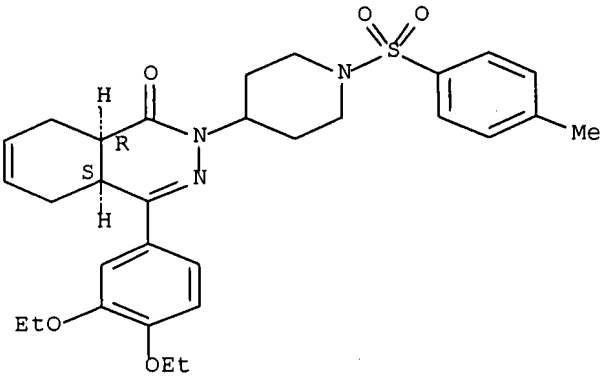
449760-50-3 449760-51-4 449760-52-5
449760-53-6 449760-54-7 449760-55-8
449760-56-9 449760-57-0 449760-58-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for treatment of disease)

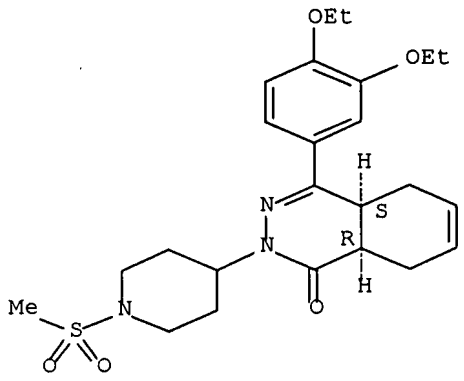
RN 449760-14-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



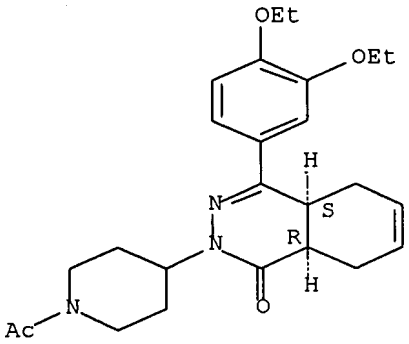
RN 449760-15-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



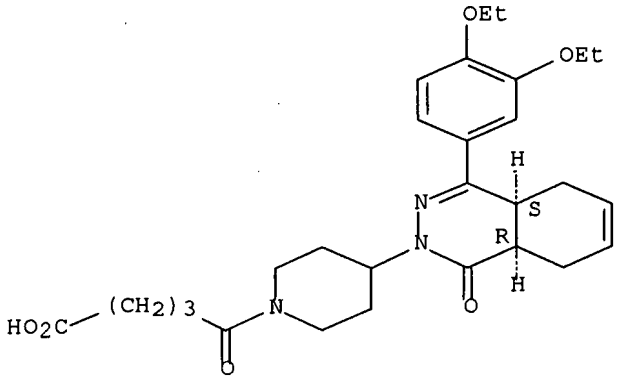
RN 449760-16-1 HCAPLUS
CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



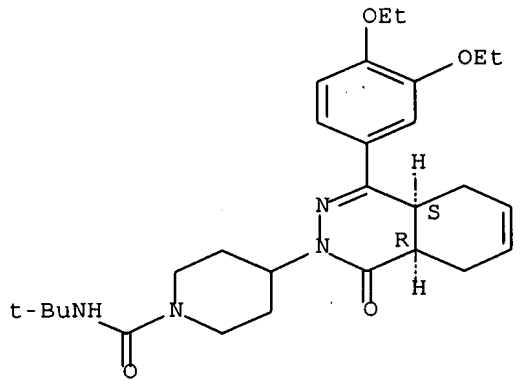
RN 449760-17-2 HCAPLUS
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



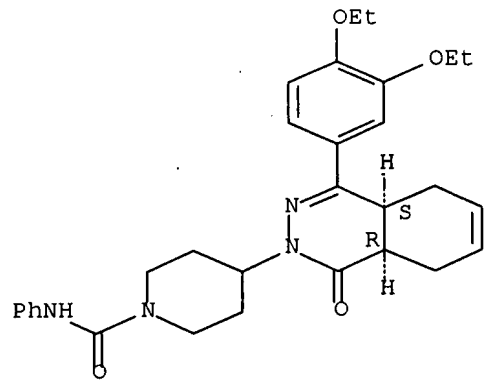
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



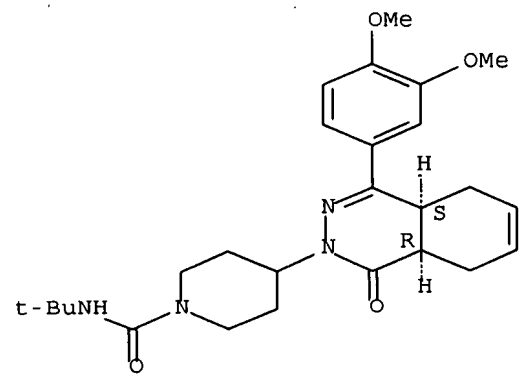
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



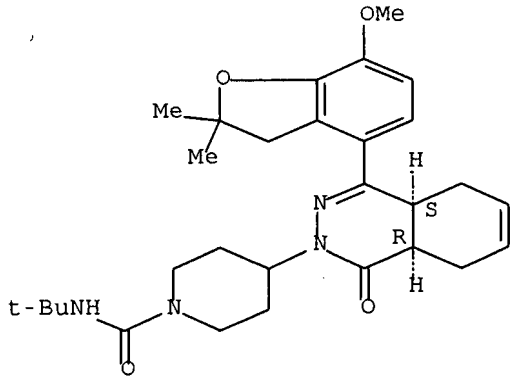
RN 449760-21-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

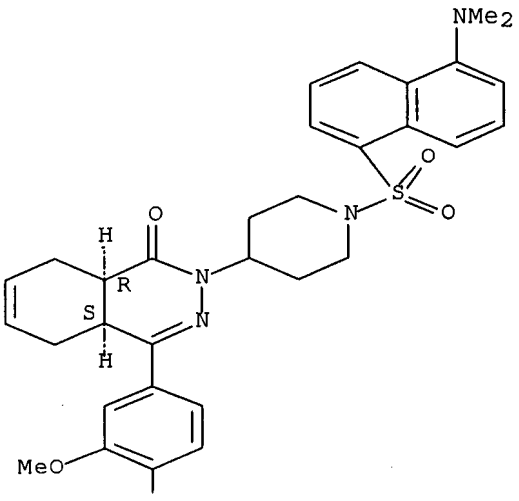
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

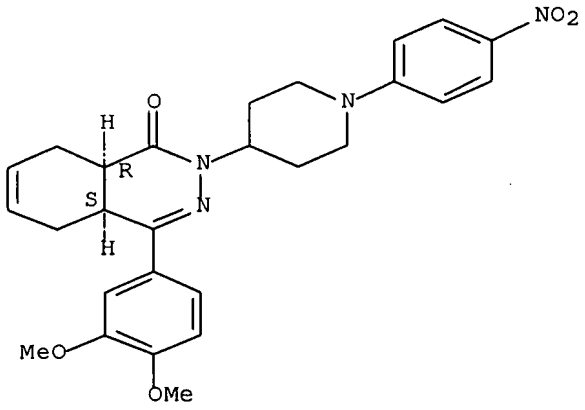
PAGE 1-A



OMe

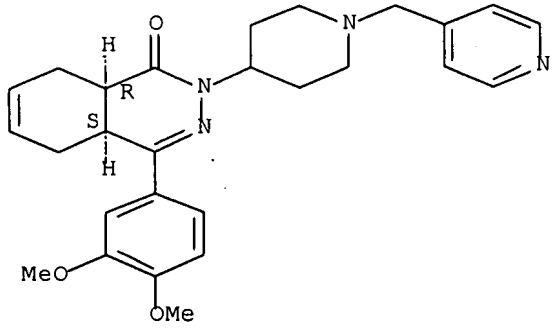
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



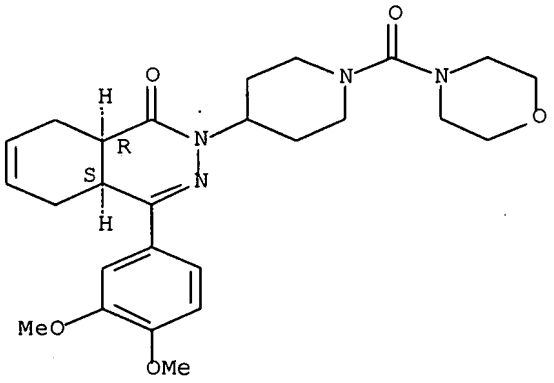
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



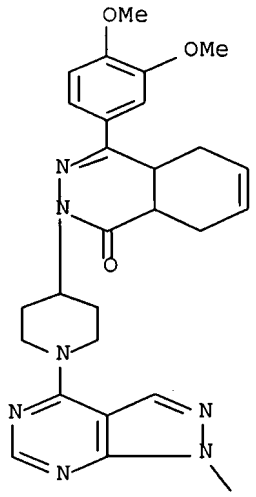
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A

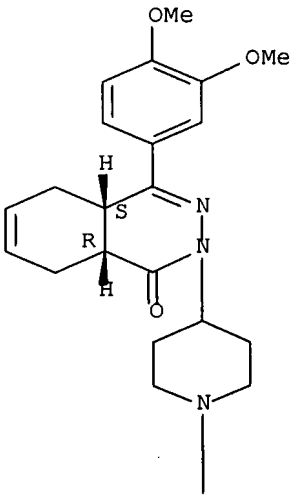


PAGE 2-A

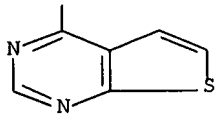
RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

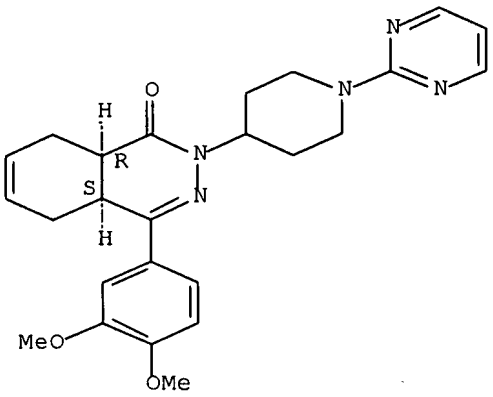


PAGE 2-A



RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

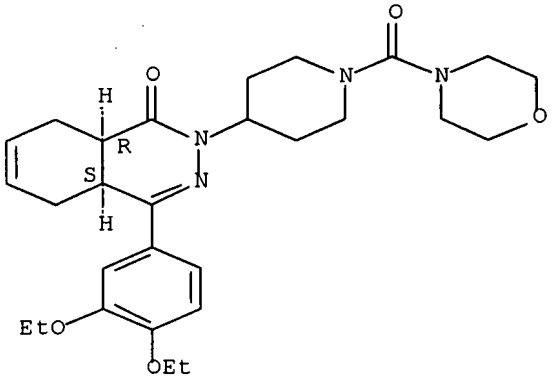
Absolute stereochemistry.



RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

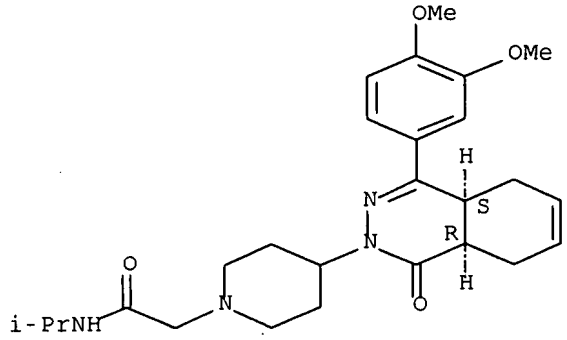
oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



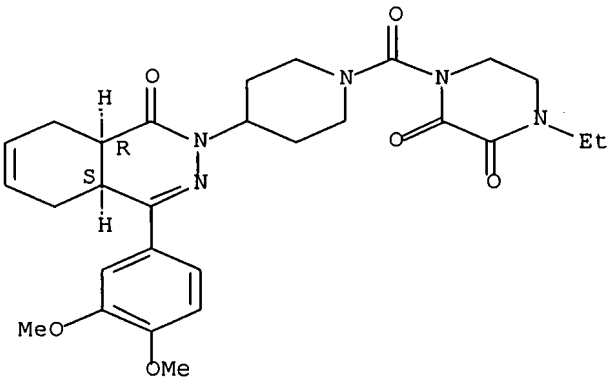
RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



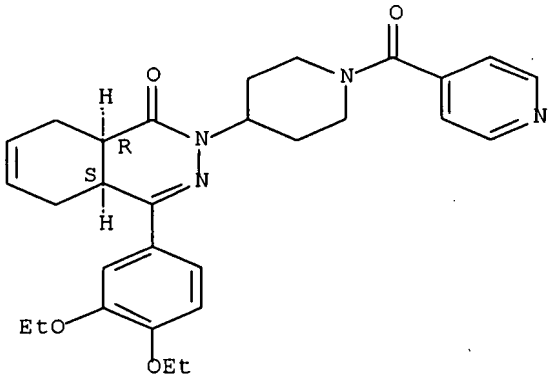
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



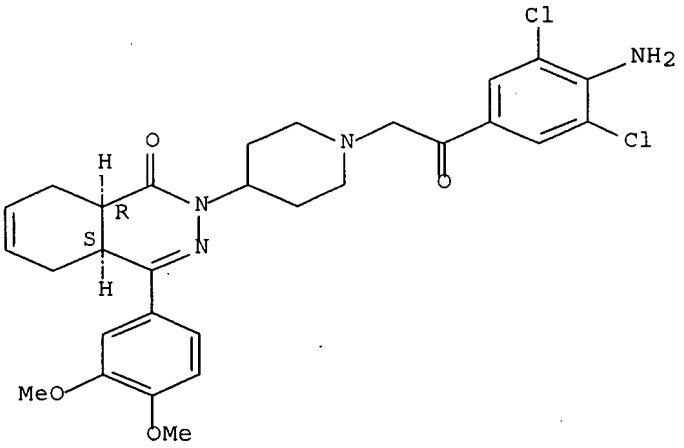
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



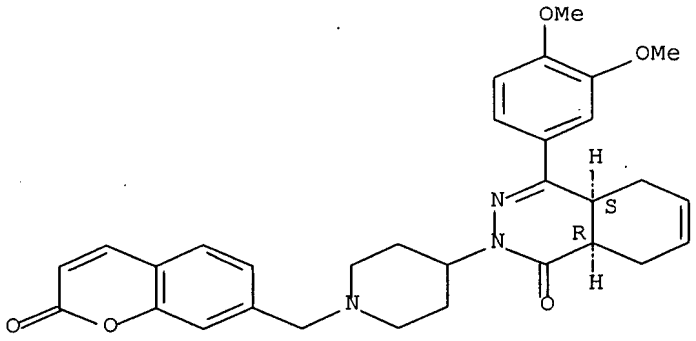
RN 449760-48-9 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



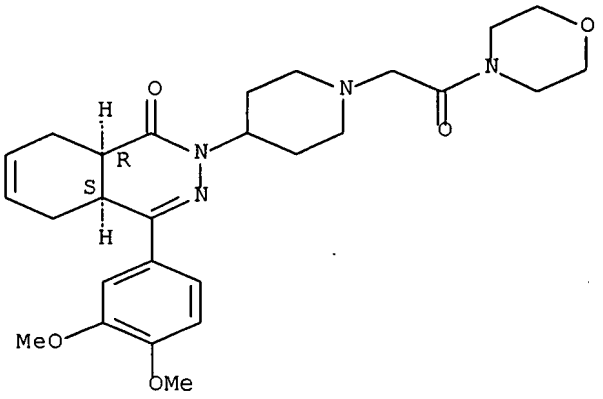
RN 449760-49-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



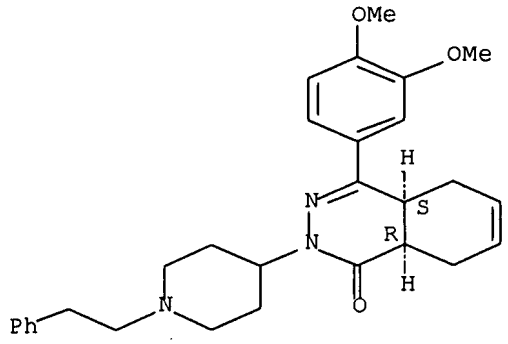
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



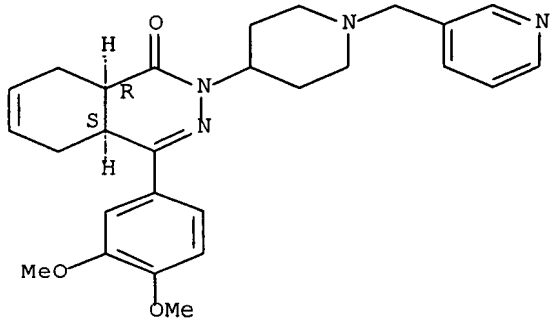
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



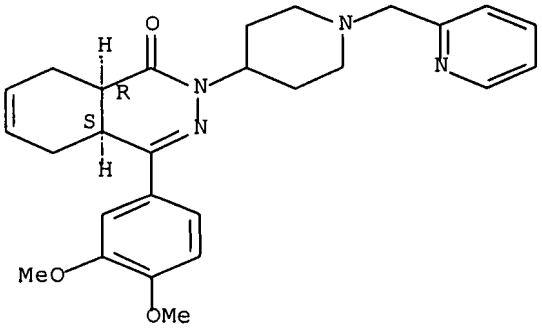
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



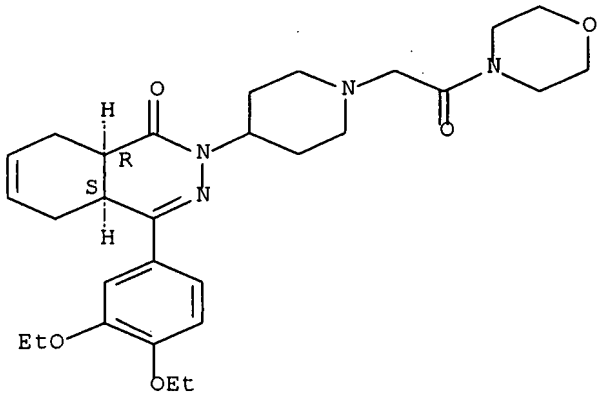
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



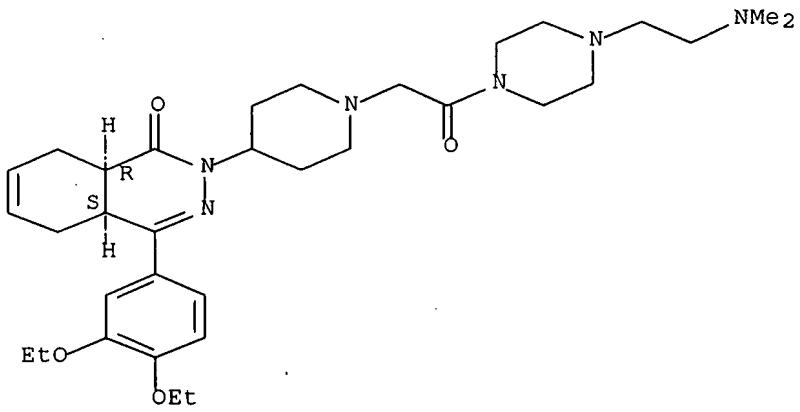
RN 449760-54-7 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



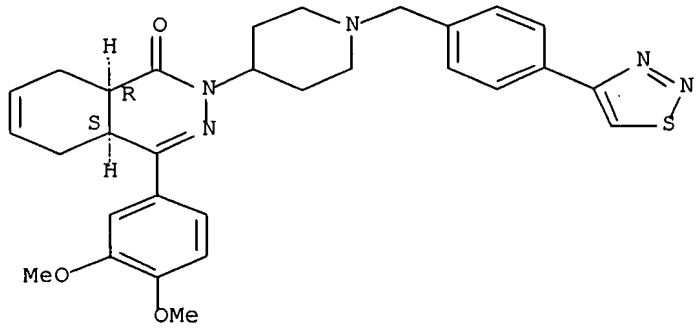
RN 449760-55-8 HCAPLUS
CN 1-Piperazineethanamine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



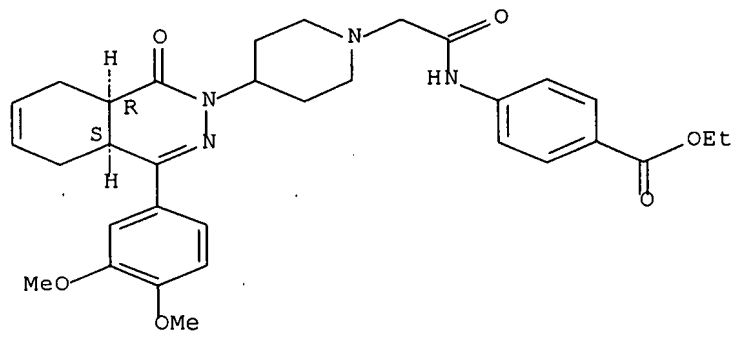
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



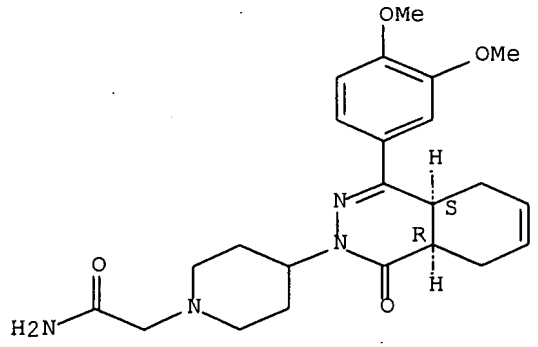
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-50
ICS A61K031-00; A61K031-4427; A61K031-275; A61K031-19; A61P011-00; A61P019-02; A61P017-06
CC 1-7 (**Pharmacology**)
IT 153259-65-5, Cilomilast 257892-33-4, AWD 12-281 **449760-14-9**
449760-15-0 449760-16-1 449760-17-2
449760-19-4 449760-20-7 449760-21-8
449760-22-9 449760-23-0 449760-24-1
449760-25-2 449760-26-3 449760-28-5
449760-29-6 449760-30-9 449760-35-4
449760-40-1 449760-42-3 449760-47-8
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449760-51-4 449760-52-5 449760-53-6
449760-54-7 449760-55-8 449760-56-9
449760-57-0 449760-58-1
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition comprising a PDE4 inhibitor and IL-1 trap for treatment of disease)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:995956 HCAPLUS Full-text
DOCUMENT NUMBER: 141:416024
TITLE: Composition comprising a PDE4 inhibitor and a TNFα antagonist
INVENTOR(S): Barsig, Johannes; Weimar, Christian
PATENT ASSIGNEE(S): Altana Pharma AG, Germany
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098578	A2	20041118	WO 2004-EP50750	20040510 <--
WO 2004098578	A3	20041229		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2003-10593 A 20030512 <--

ED Entered STN: 19 Nov 2004

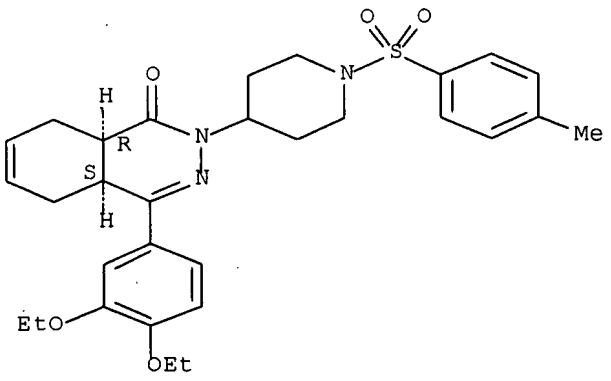
AB The invention relates to the combined administration of a PDE4 inhibitor and a TNFα antagonist selected from the group consisting of infliximab, adalimumab, cdp870 and cdp571 for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNFα) activity is detrimental.

IT **449760-14-9 449760-15-0 449760-16-1**
449760-17-2 449760-19-4 449760-20-7
449760-21-8 449760-22-9 449760-23-0
449760-24-1 449760-25-2 449760-26-3
449760-28-5 449760-29-6 449760-30-9
449760-35-4 449760-40-1 449760-42-3
449760-47-8 449760-48-9 449760-49-0
449760-50-3 449760-51-4 449760-52-5
449760-53-6 449760-54-7 449760-55-8
449760-56-9 449760-57-0 449760-58-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical injections containing phosphodiesterase 4 inhibitors in combination with TNFα antagonists for treatment of arthritis and other diseases)

RN 449760-14-9 HCAPLUS

CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

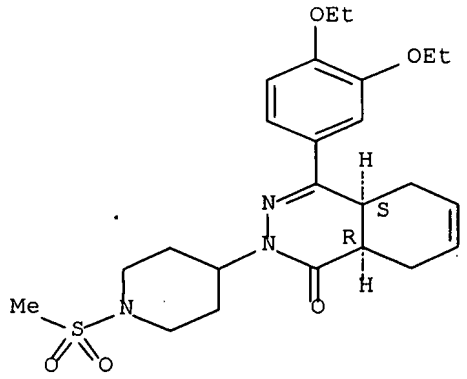
Absolute stereochemistry.



RN 449760-15-0 HCAPLUS

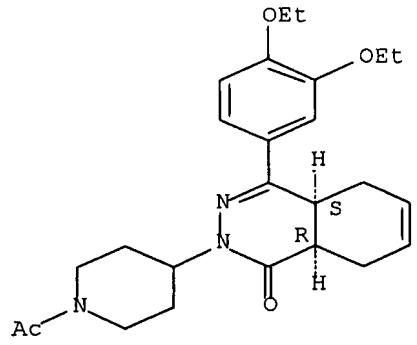
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



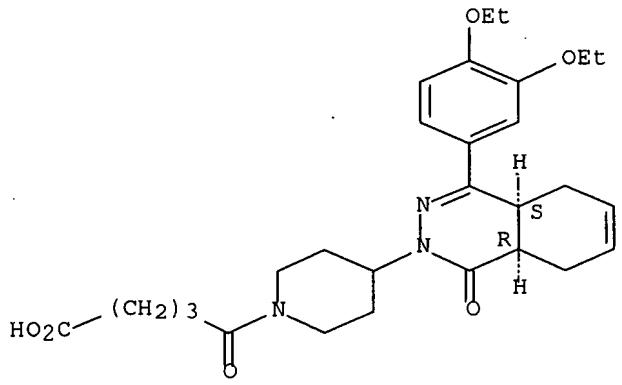
RN 449760-16-1 HCAPLUS
CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



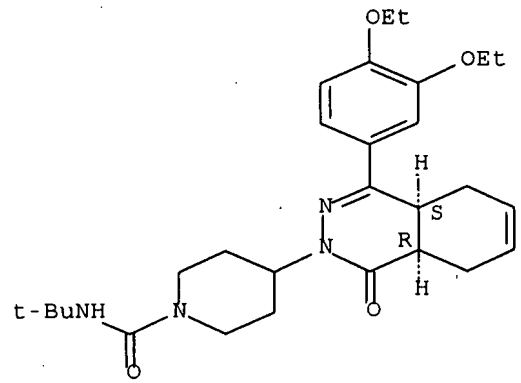
RN 449760-17-2 HCAPLUS
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



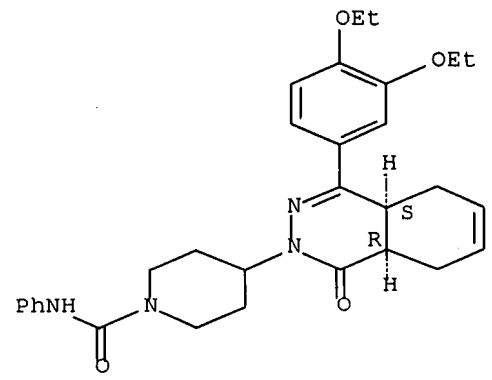
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



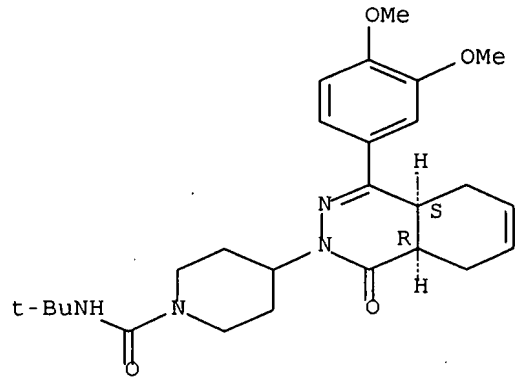
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



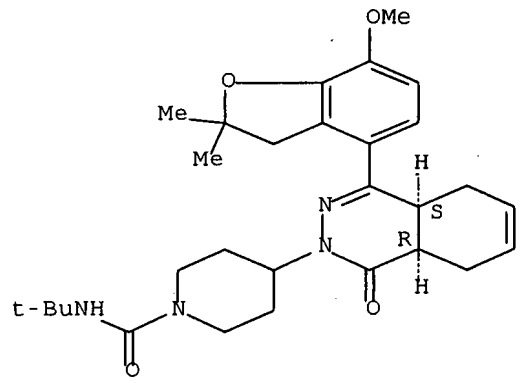
RN 449760-21-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

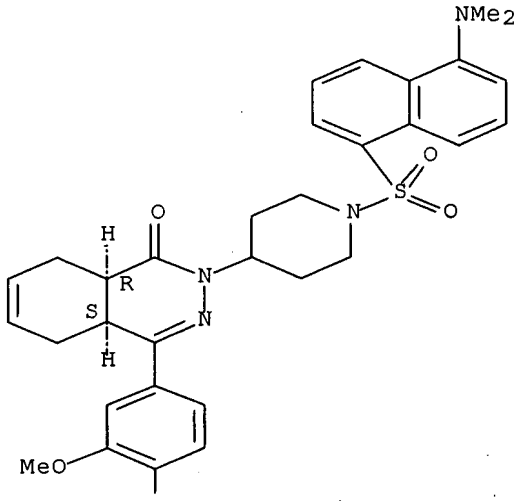
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

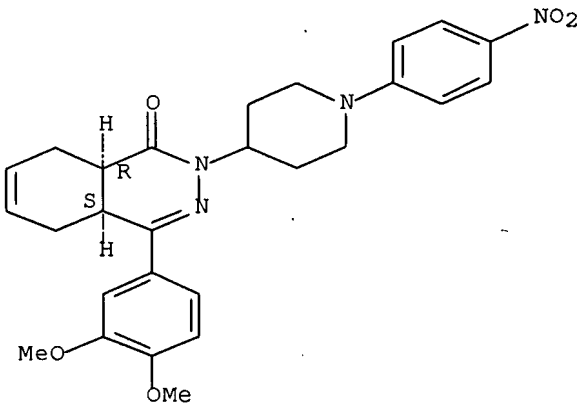


PAGE 2-A

OMe

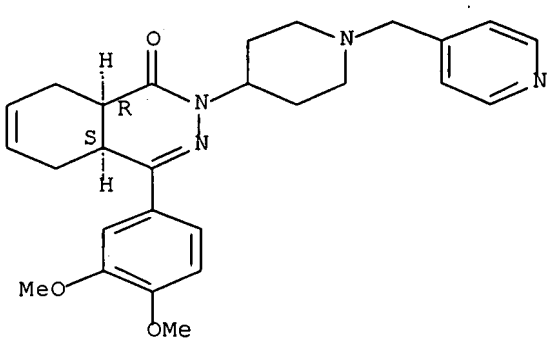
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



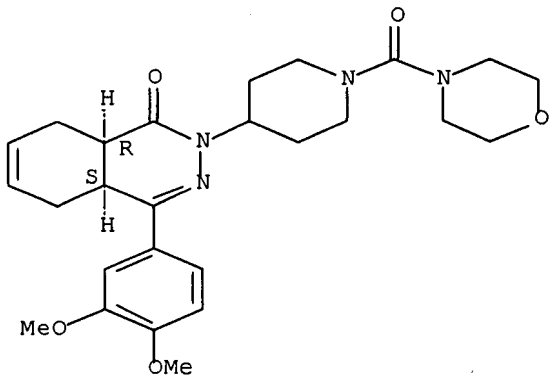
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



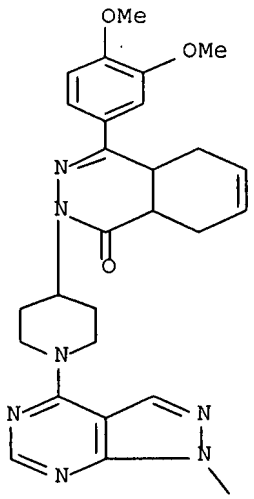
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A



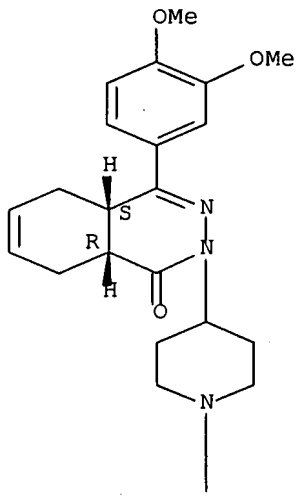
PAGE 2-A

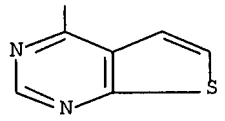
Me

RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

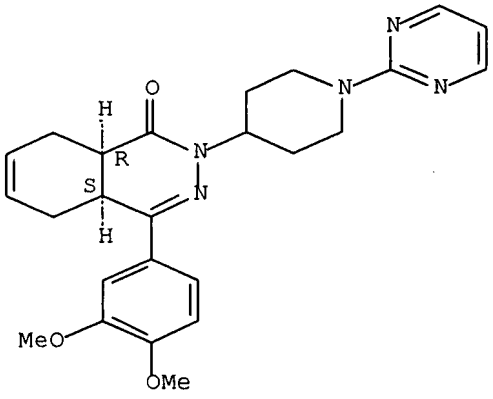
PAGE 1-A





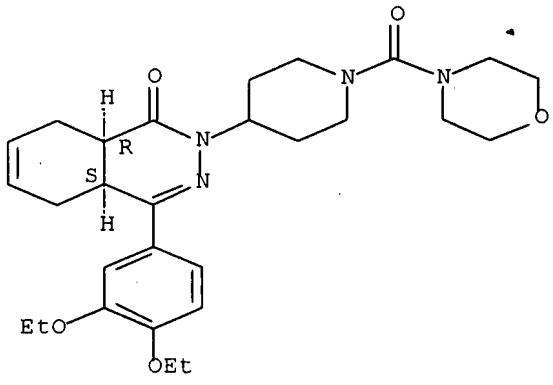
RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

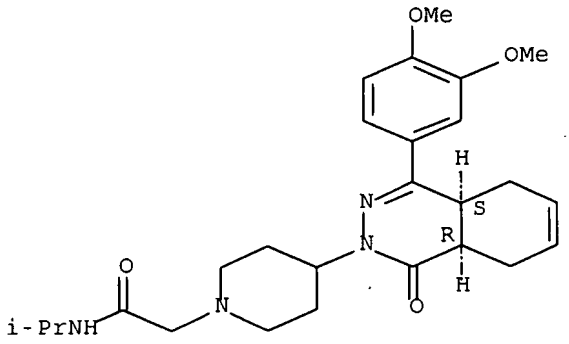
Absolute stereochemistry.



RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-

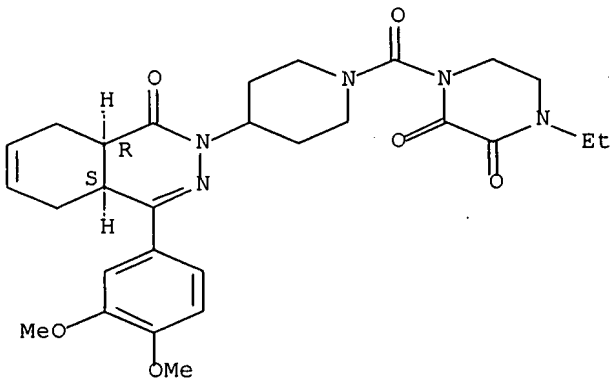
tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



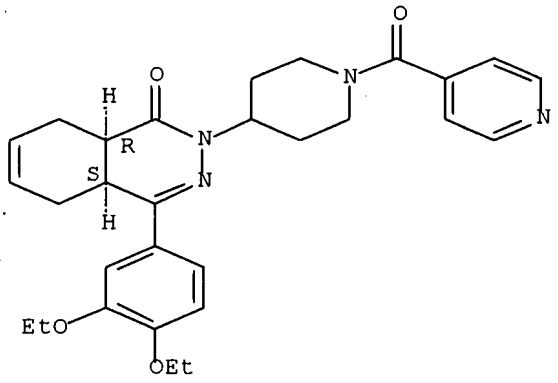
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



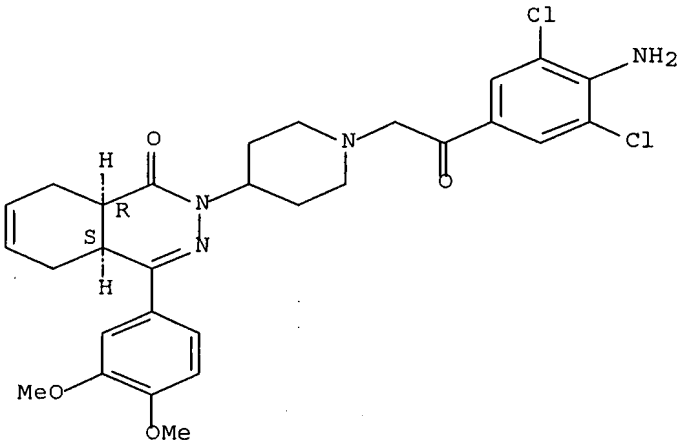
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



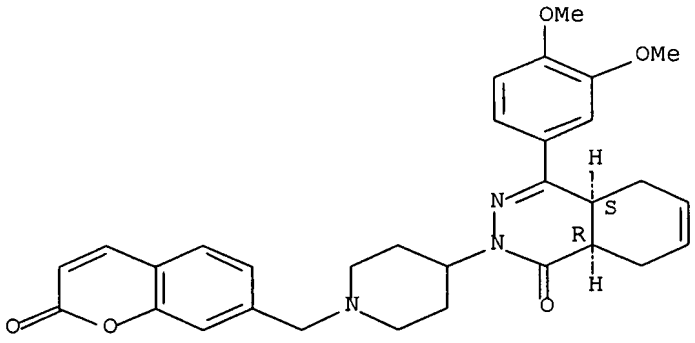
RN 449760-48-9 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



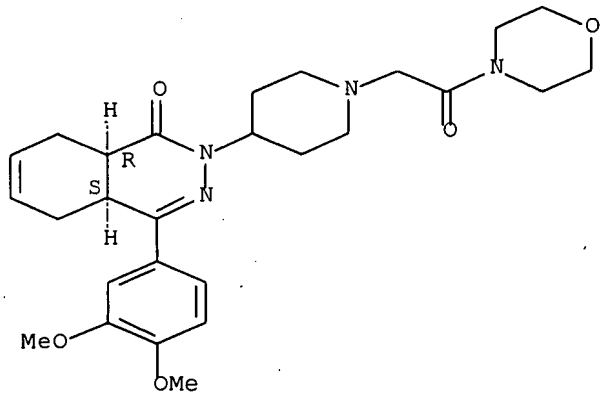
RN 449760-49-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



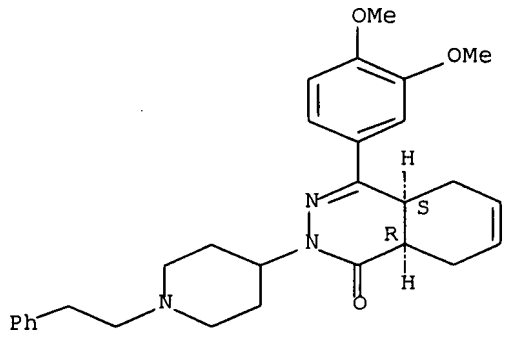
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



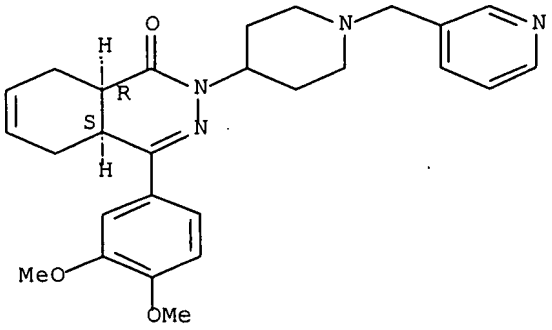
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



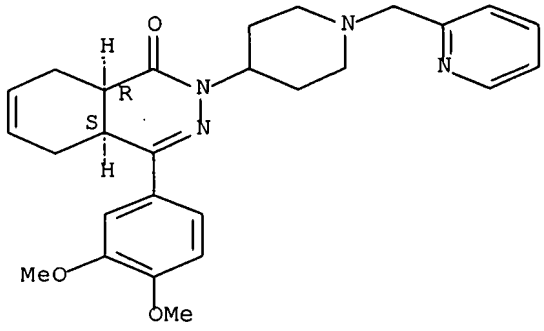
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



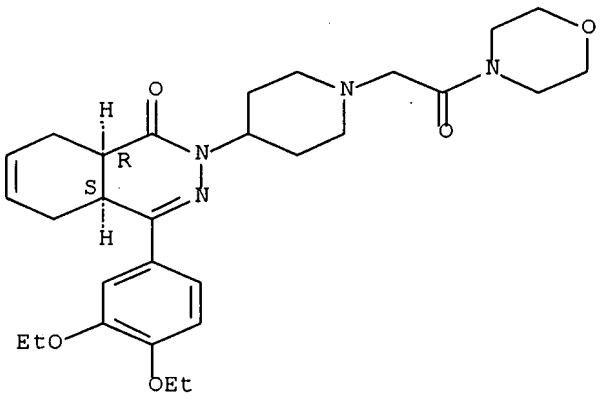
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



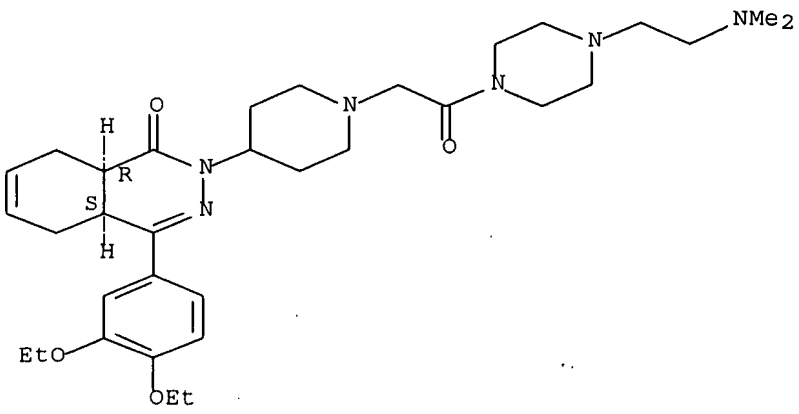
RN 449760-54-7 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



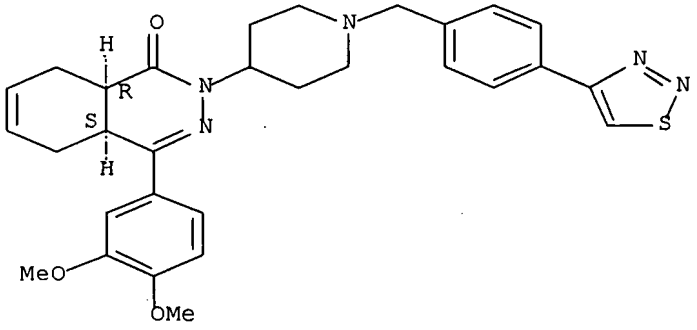
RN 449760-55-8 HCAPLUS
CN 1-Piperazineethanamine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



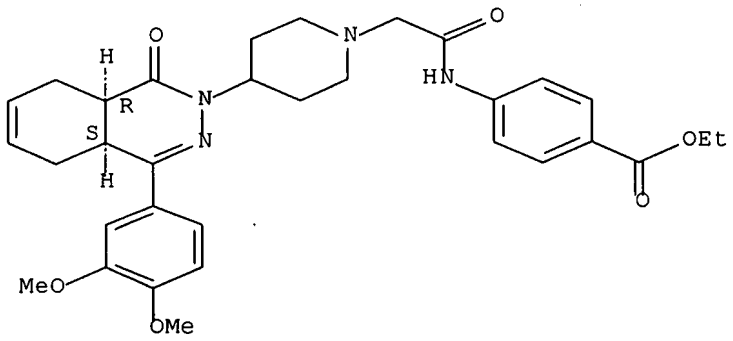
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



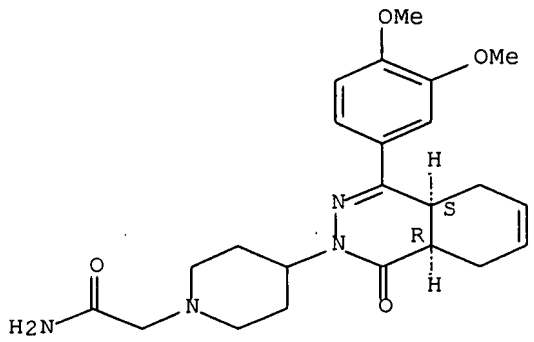
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-00
CC 63-6 (**Pharmaceuticals**)
IT 170277-31-3, Infliximab 331731-18-1, Adalimumab 336128-48-4, Cdp571
428863-50-7, CDP 870 **449760-14-9 449760-15-0**
449760-16-1 449760-17-2 449760-19-4
449760-20-7 449760-21-8 449760-22-9
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449760-55-8 449760-56-9 449760-57-0
449760-58-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical injections containing phosphodiesterase 4 inhibitors in combination with TNFα antagonists for treatment of arthritis and other diseases)

L18 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:610086 HCAPLUS Full-text
DOCUMENT NUMBER: 141:134069
TITLE: PDE4 inhibitors for the treatment of neoplasms of lymphoid cells
INVENTOR(S): Hatzelmann, Armin; Tenor, Hermann; Gekeler, Volker; Sanders, Karl; Garattini, Enrico; Braunger, Juergen; Schudt, Christian
PATENT ASSIGNEE(S): Altana Pharma Ag, Germany
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

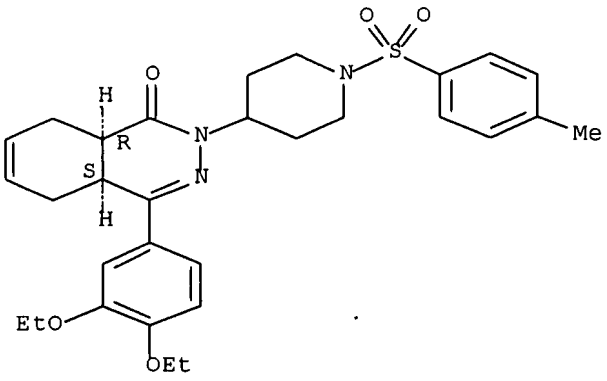
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004062671	A2	20040729	WO 2004-EP196		20040114 <--
WO 2004062671	A3	20050127			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ					
AU 2004204355	A1	20040729	AU 2004-204355		20040114 <--
CA 2512819	A1	20040729	CA 2004-2512819		20040114 <--
EP 1587512	A2	20051026	EP 2004-701902		20040114 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2006515367	T	20060525	JP 2006-500561		20040114 <--
US 2006148804	A1	20060706	US 2005-542088		20050713 <--
PRIORITY APPLN. INFO.:			EP 2003-787	A	20030114 <--
			WO 2004-EP196	W	20040114 <--

OTHER SOURCE(S): MARPAT 141:134069
ED Entered STN: 30 Jul 2004
AB The invention relates to the use of certain PDE4 inhibitors alone or in combination with one or more differentiation inducing agents and/or an agent effective in raising intracellular concns. of cAMP or a stable analog of cAMP in the preparation of pharmaceutical compns. for the treatment of neoplasms of lymphoid cells.
IT **449760-14-9 449760-15-0 449760-16-1**

449760-17-2 449760-19-4 449760-20-7
449760-21-8 449760-22-9 449760-23-0
449760-24-1 449760-25-2 449760-26-3
449760-28-5 449760-29-6 449760-30-9
449760-35-4 449760-40-1 449760-42-3
449760-47-8 449760-48-9 449760-49-0
449760-50-3 449760-51-4 449760-52-5
449760-53-6 449760-56-9 449760-57-0
449760-58-1 596102-01-1 596102-07-7
596102-09-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 (PDE4) inhibitors for treatment of neoplasms of lymphoid cells in combination with differentiation inducers and agents that increase cAMP levels or cAMP analogs)

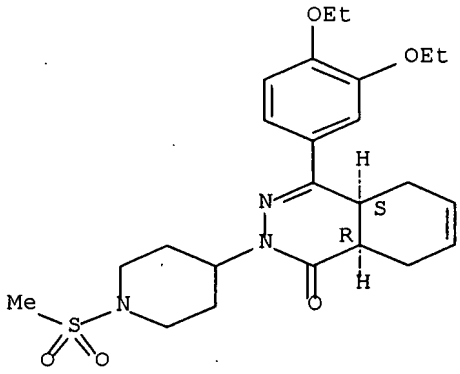
RN 449760-14-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



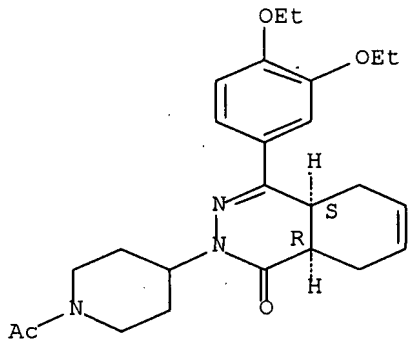
RN 449760-15-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



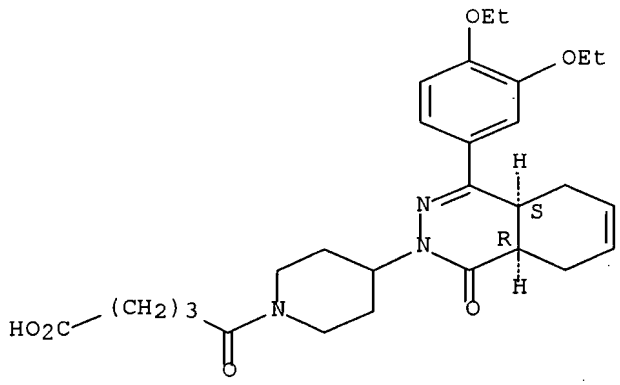
RN 449760-16-1 HCAPLUS
CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



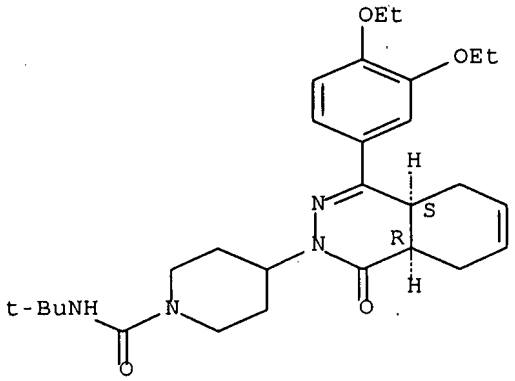
RN 449760-17-2 HCAPLUS
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



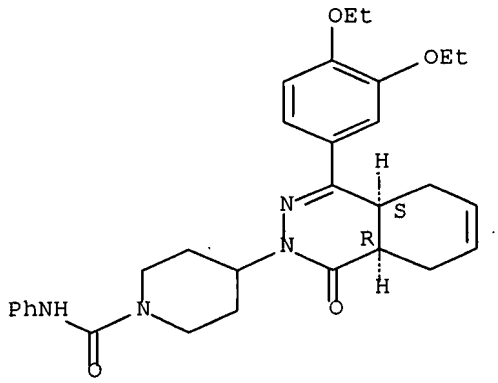
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



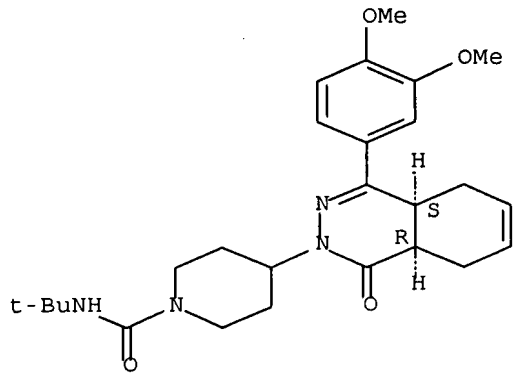
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



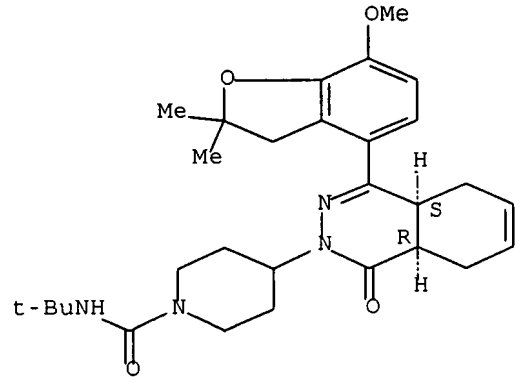
RN 449760-21-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

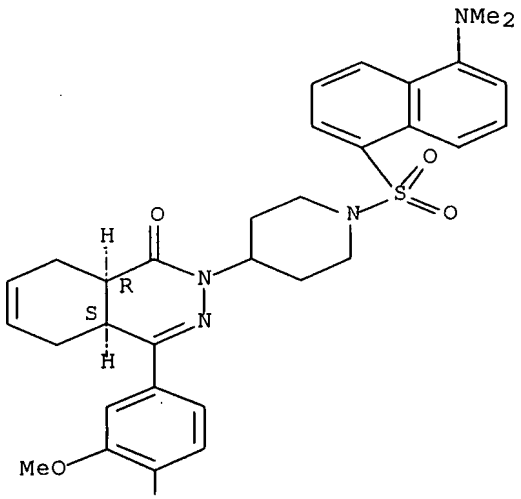
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

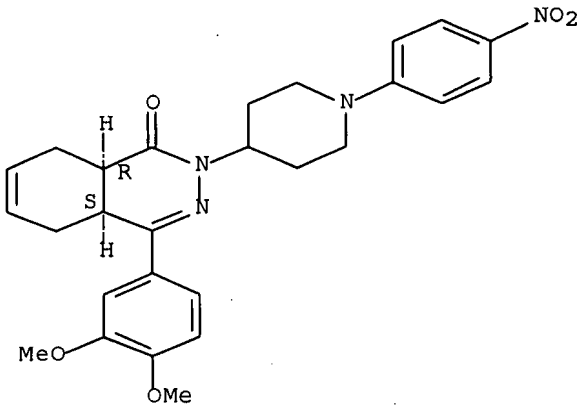
PAGE 1-A



OMe

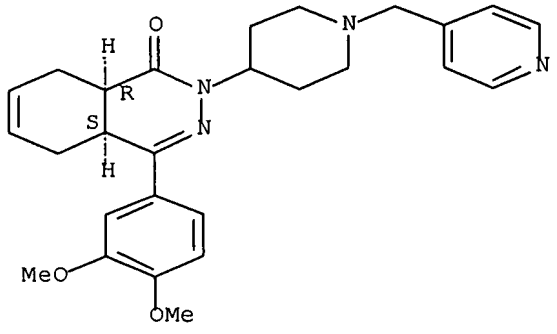
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



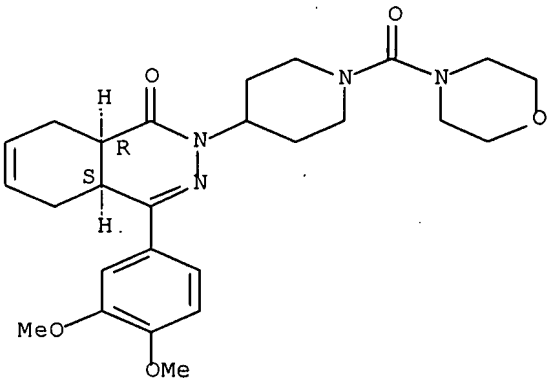
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



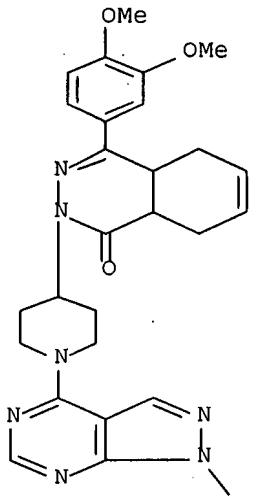
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A



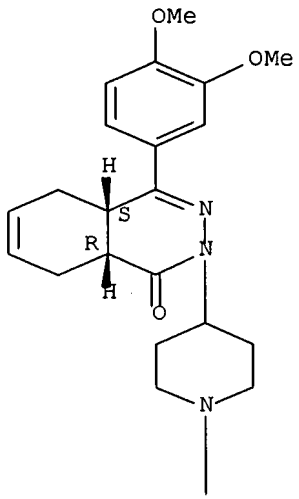
PAGE 2-A

Me

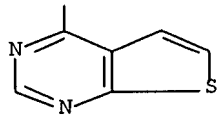
RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

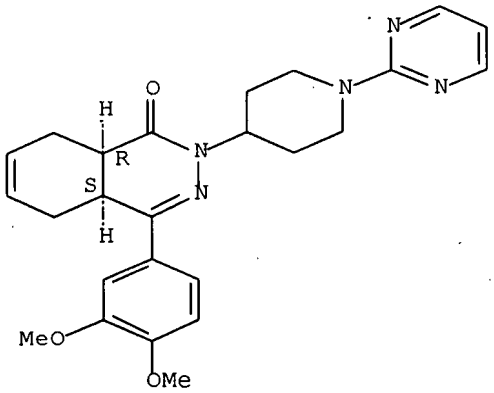


PAGE 2-A



RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

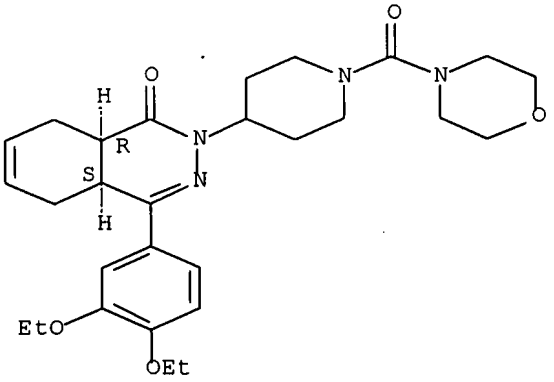
Absolute stereochemistry.



RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

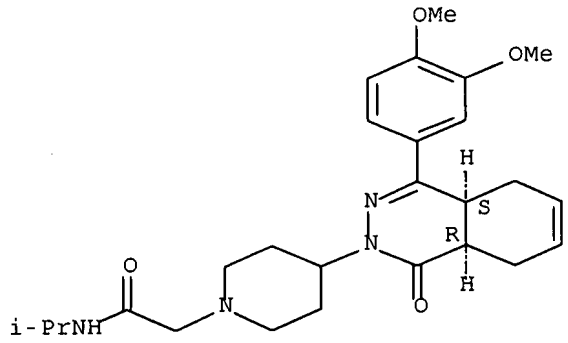
oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



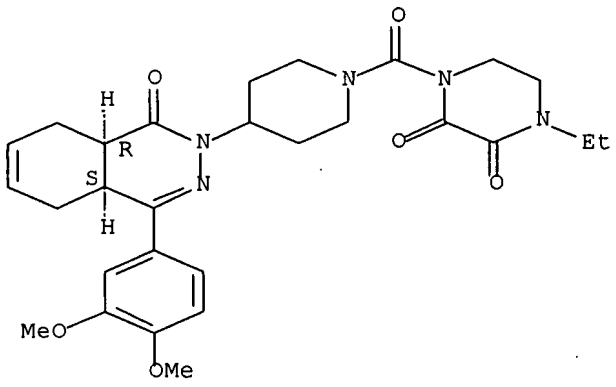
RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



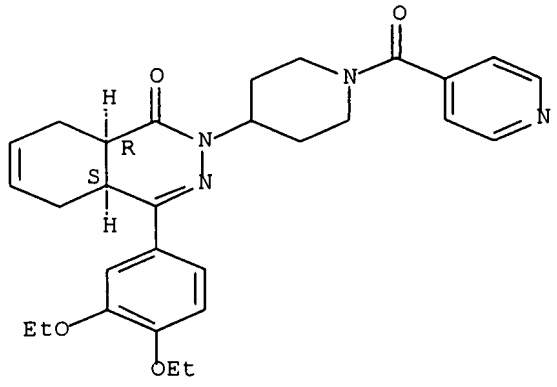
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



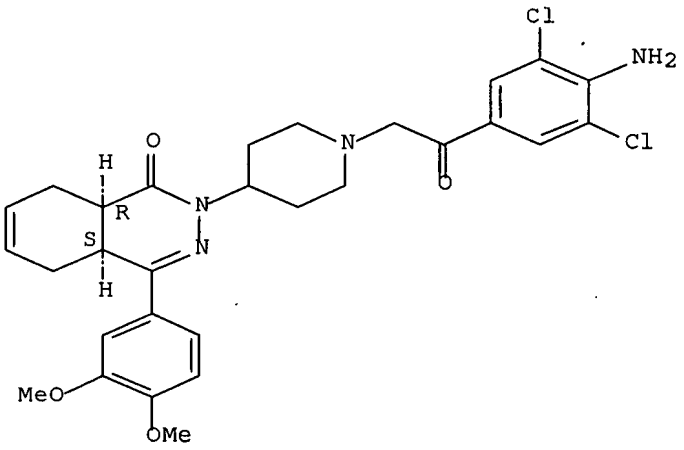
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



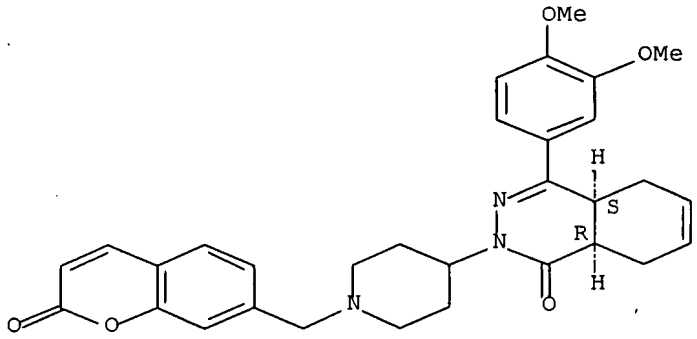
RN 449760-48-9 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



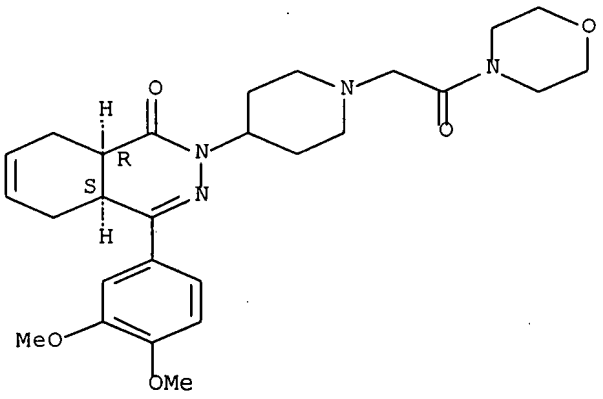
RN 449760-49-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



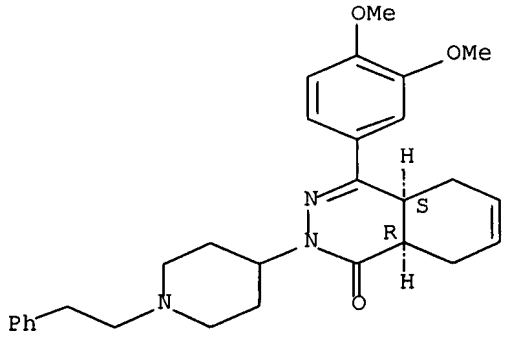
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



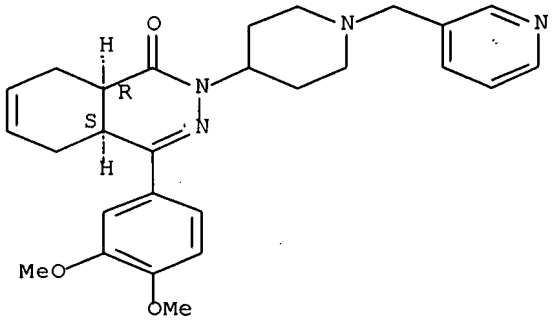
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



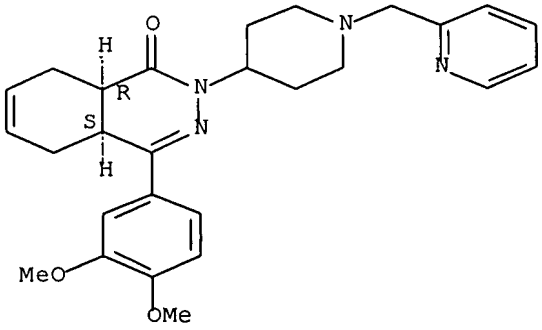
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



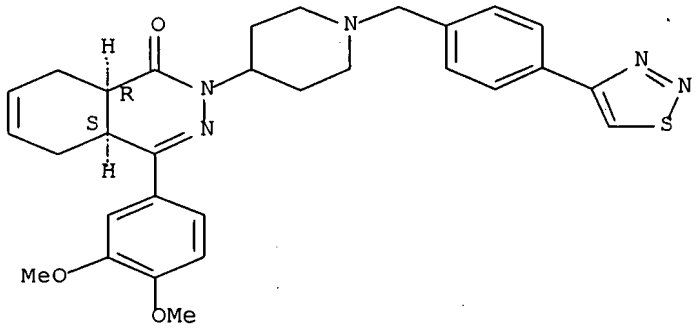
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



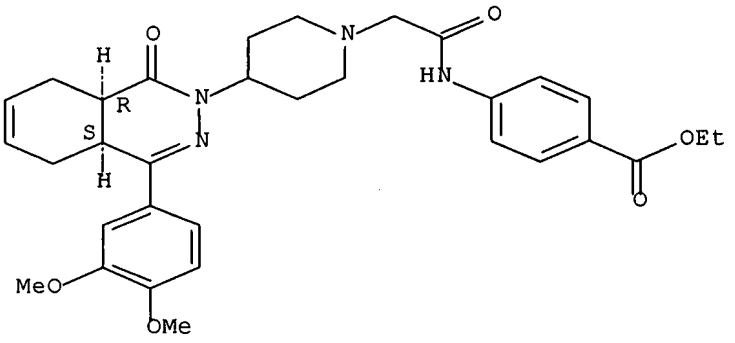
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



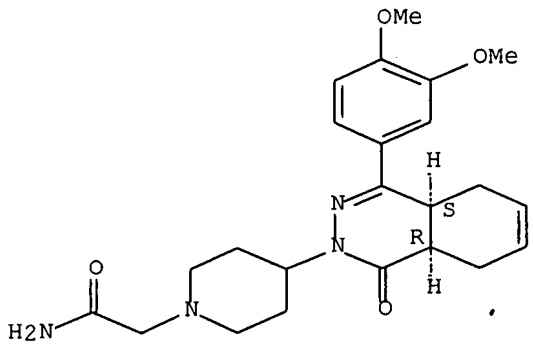
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

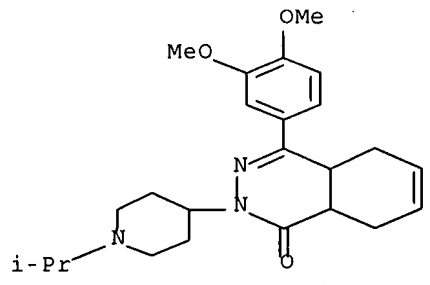


RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.

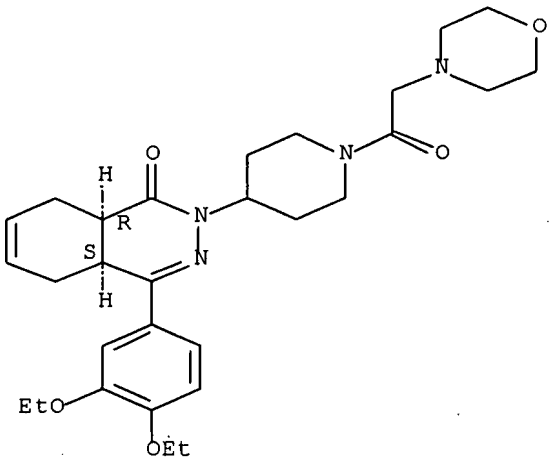


RN 596102-01-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methylethyl)-4-piperidinyl]- (CA INDEX NAME)



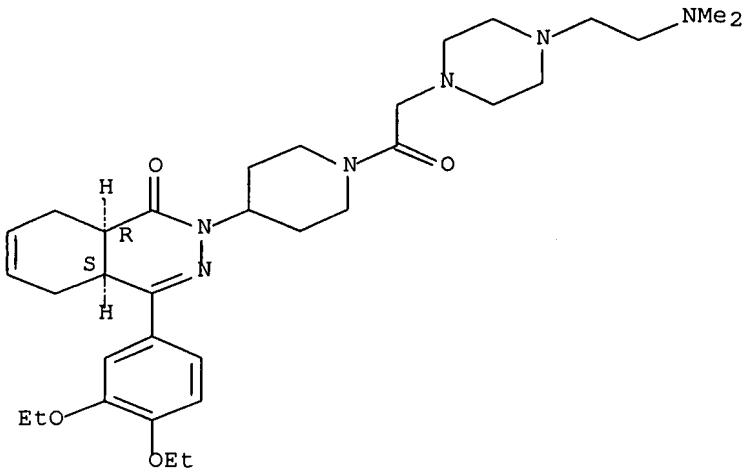
RN 596102-07-7 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-morpholinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596102-09-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[4-[2-(dimethylamino)ethyl]-1-piperazinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-502
ICS A61P035-02; A61P035-00; A61K031-00
CC 1-6 (**Pharmacology**)
IT 60-92-4D, CAMP, analogs 135637-46-6, Atizoram 136145-07-8, Arofylline 144035-83-6, Piclamilast 153259-65-5, Cilomilast 162278-09-3, V-11294A 162401-32-3, Roflumilast 192819-27-5, CDC-801 257892-33-4, AWD-12-281 292135-78-5 329306-27-6, Lirimilast 337359-69-0 337359-70-3 337359-71-4 337359-72-5 337359-73-6 337359-74-7 337359-75-8 337359-76-9 337532-27-1 337532-29-3 444658-74-6, CDC-998 444659-40-9, IC-485 444659-42-1, KW4490 444659-43-2, SCH-351591 444659-44-3, AWD-12-343 **449760-14-9 449760-15-0**

449760-16-1 449760-17-2 449760-19-4
449760-20-7 449760-21-8 449760-22-9
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596102-01-1 596102-07-7 596102-09-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 (PDE4) inhibitors for treatment of neoplasms of lymphoid cells in combination with differentiation inducers and agents that increase cAMP levels or cAMP analogs)

L18 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182870 HCAPLUS Full-text
DOCUMENT NUMBER: 140:217652
TITLE: Preparation of pyrrolidinedione substituted piperidine-phthalazones as cyclic nucleotide phosphodiesterase-4 (PDE4) inhibitors
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christiaans, Johannes A. M.; Menge, Wiro M. P. B.; Sterk, Geert Jan
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018457	A1	20040304	WO 2003-EP8675	20030806 <--
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2494613	A1	20040304	CA 2003-2494613	20030806 <--
AU 2003258576	A1	20040311	AU 2003-258576	20030806 <--
EP 1537100	A1	20050608	EP 2003-792257	20030806 <--
EP 1537100	B1	20070425		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003013330	A	20050614	BR 2003-13330	20030806 <--
CN 1671695	A	20050921	CN 2003-818520	20030806 <--
JP 2006500370	T	20060105	JP 2004-530086	20030806 <--
AT 360627	T	20070515	AT 2003-792257	20030806 <--
IN 2005MN00028	A	20050218	IN 2005-MN28	20050112 <--
MX 2005PA01354	A	20050428	MX 2005-PA1354	20050202 <--
US 2006160813	A1	20060720	US 2005-523412	20051107 <--
US 7220746	B2	20070522		
PRIORITY APPLN. INFO.:			EP 2002-17977 A	20020810 <--
			WO 2003-EP8675 W	20030806 <--

OTHER SOURCE(S): MARPAT 140:217652
ED Entered STN: 05 Mar 2004

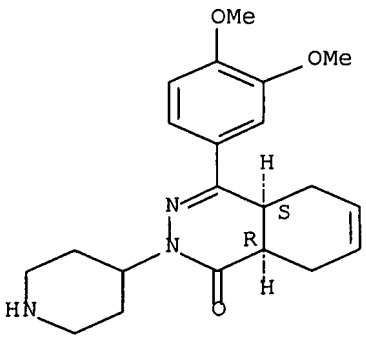
AB 1-(4-Piperidinyl)-4a,5,8,8a-tetrahydro-1H-phthalazin-1-one compds. of formula (I) [R1 and R2 are both H or together form an addnl. bond; R3 = a Ph derivative of formulas Q or Q1; R4 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; R5 = C1-4 alkoxy, C3-7 cycloalkoxy, C3-7 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R6 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; wherein R7 = C1-4 alkyl; R8 = H, C1-4 alkyl; or R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulfur atom; R9 = CO(CH2)n-R10; wherein R10 = 2,5-dioxopyrrolidin-1-yl; n = an integer of 1-4] and the salts of these compds. These compds. are useful in the preparation of pharmaceutical compns. for the treatment of an illness treatable by the administration of a PDE4 inhibitor, in particular airway disorders. Thus, 1-[2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo- 4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]piperidin-1-yl]-2- oxoethyl]pyrrolidine-2,5-dione >. Thus, a mixture of 1 g (4aS,8aR)-2-[1-(2-Chloroethanoyl)piperidin-4-yl]-4-(3,4-dimethoxyphenyl)- 4a,5,8,8a-tetrahydro-2H-phthalazin-1-one, 0.4 g succinimide, 1 g potassium carbonate in 20 mL DMF was stirred for 18 h at room temperature to give, after workup and silica gel chromatog. and crystallization from EtOAc, 1-[2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H- phthalazin-2-yl]piperidin-1-yl]-2-oxoethyl]pyrrolidine-2,5-dione (II). II showed -logIC50(mol/L) of 10.66 against PDE4.

IT **380226-97-1P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
380227-13-4P, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
666735-57-5P 666735-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrrolidinedione substituted piperidine-phthalazones as cyclic nucleotide phosphodiesterase-4 (PDE4) inhibitors for treating airway diseases)

RN 380226-97-1 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

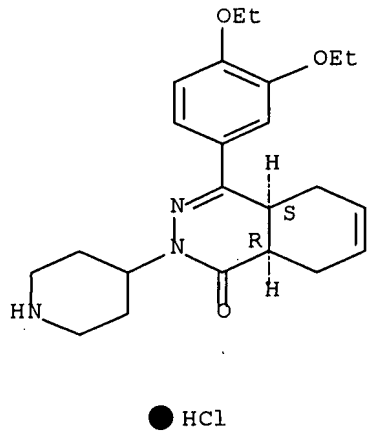


● HCl

RN 380227-13-4 HCAPLUS

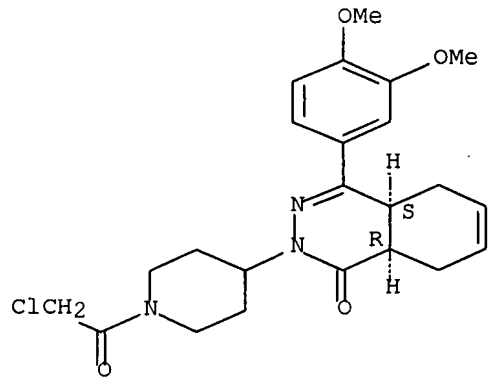
CN 1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



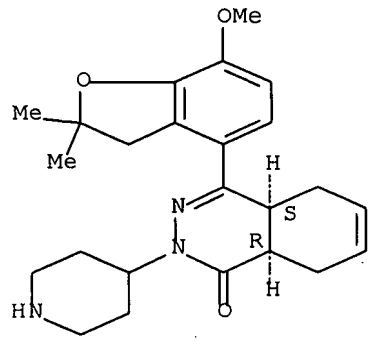
RN 666735-57-5 HCAPLUS
CN Piperidine, 1-(chloroacetyl)-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 666735-60-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



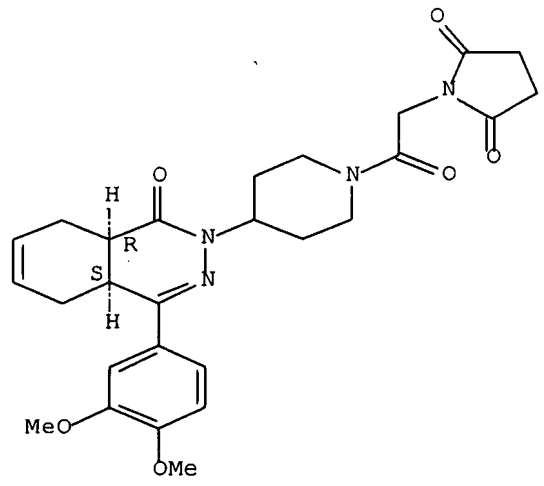
● HCl

IT **666735-56-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinedione substituted piperidine-phthalazones as cyclic nucleotide phosphodiesterase-4 (PDE4) inhibitors for treating airway diseases)

RN 666735-56-4 HCAPLUS

CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(2,5-dioxo-1-pyrrolidinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07D401-14
ICS A61K031-502; A61P011-00

CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**, 7

IT 210467-67-7P, cis-2-(3,4-Dimethoxybenzoyl)-1,2,3,6-tetrahydrobenzoic acid 227967-42-2P, cis-2-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-carbonyl)-1,2,3,6-tetrahydrobenzoic acid 244077-33-6P,

cis-2-(3,4-Diethoxybenzoyl)-1,2,3,6-tetrahydrobenzoic acid
380226-97-1P, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride 380226-98-2P, Piperidin-4-ylhydrazine dihydrochloride 380226-99-3P 380227-00-9P
380227-13-4P, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
666735-57-5P 666735-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrrolidinedione substituted piperidine-phthalazones as cyclic nucleotide phosphodiesterase-4 (PDE4) inhibitors for treating airway diseases)

IT **666735-56-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyrrolidinedione substituted piperidine-phthalazones as cyclic nucleotide phosphodiesterase-4 (PDE4) inhibitors for treating airway diseases)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182864 HCAPLUS Full-text
DOCUMENT NUMBER: 140:217651
TITLE: Preparation of piperidinylpyridazinones as inhibitors of phosphodiesterase PDE4 or PDE3/4 inhibitors.
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christiaans, Johannes A. M.; Menge, Wiro M. P. B.; Sterk, Geert Jan
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

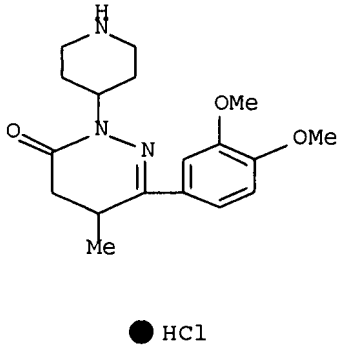
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 2004018451	A1	20040304	WO 2003-EP8677		20030806	<--
WO 2004018451	A8	20040506				
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW						
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR						
CA 2494650	A1	20040304	CA 2003-2494650		20030806	<--
AU 2003251693	A1	20040311	AU 2003-251693		20030806	<--
EP 1556369	A1	20050727	EP 2003-792259		20030806	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK						
JP 2005538138	T	20051215	JP 2004-530088		20030806	<--
US 2006167001	A1	20060727	US 2005-523112		20050203	<--
PRIORITY APPLN. INFO.:			EP 2002-17976	A	20020810	<--
			WO 2003-EP8677	W	20030806	<--

OTHER SOURCE(S): MARPAT 140:217651
ED Entered STN: 05 Mar 2004

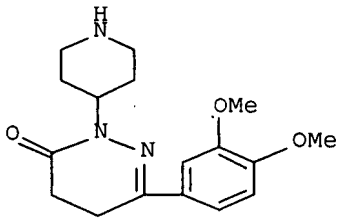
AB Title compds. [I; R1, R2 = H, alkyl; R3 = Q1, Q2; R4 = (fluoro)alkoxy; R5, R6 = cycloalkoxy, cycloalkylmethoxy, (fluoro)alkoxy; R7 = alkyl; R8 = H, alkyl; R7R8 = atoms to form a 5-7 membered ring optionally interrupted by O, S; R9 = alkyl, SO2R10, COR13, aryl, etc.; R10 = alkyl, 5-dimethylaminonaphthalen-1-yl, thienyl, NR16R17, (substituted) Ph, etc.; R13 = alkyl, carboxyalkyl, Ph, pyridyl, NR16R17, etc.; R16 = H, alkyl, cycloalkyl, cycloalkylmethyl, (substituted) Ph; R17 = alkyl, cycloalkyl, cycloalkylmethyl, (substituted) Ph; NR16R17 = 4-morpholinyl, 1-pyrrolidinyl, 1-piperidinyl, 1-hexahydroazepinyl, (substituted) piperazinyl], were prepared Thus, piperidin-4-ylhydrazine dihydrochloride (preparation given), 4-(3,4-dimethoxyphenyl)-3-methyl-4-oxobutyric acid, and Et3N were refluxed 18 h in PrOH to give 6-(3,4-dimethoxyphenyl)-5-methyl-2- piperidin-4-yl-4,5-dihydro-2H-pyridazin-3-one hydrochloride. I inhibited PDE4 with -log IC50 = 7.17-8.39.

IT **666750-56-7P**, 6-(3,4-Dimethoxyphenyl)-5-methyl-2-piperidin-4-yl-4,5-dihydro-2H-pyridazin-3-one hydrochloride **666750-57-8P** **666750-58-9P** **666750-59-0P** **666750-60-3P** **666750-61-4P** **666750-62-5P** **666750-63-6P** **666750-64-7P** **666750-65-8P** **666750-66-9P** **666750-67-0P** **666750-68-1P** **666750-69-2P** **666750-70-5P** **666750-71-6P** **666750-72-7P** **666750-73-8P** **666750-74-9P** **666750-75-0P** **666750-76-1P** **666750-77-2P** **666750-78-3P** **666750-79-4P** **666750-80-7P** **666750-81-8P** **666750-82-9P** **666750-83-0P** **666750-84-1P** **666750-85-2P** **666750-86-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinylpyridazinones as phosphodiesterase PDE4 or PDE3/4 inhibitors)

RN 666750-56-7 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-5-methyl-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

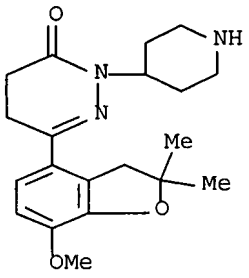


RN 666750-57-8 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



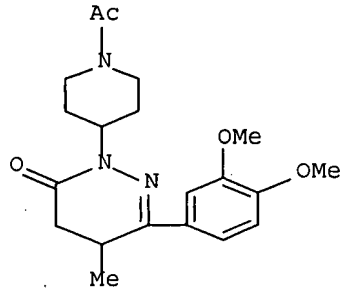
● HCl

RN 666750-58-9 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

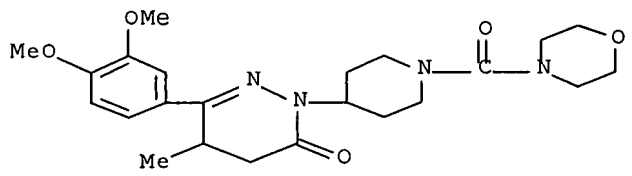


● HCl

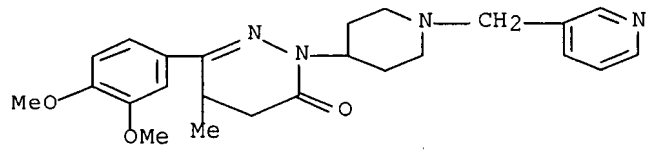
RN 666750-59-0 HCAPLUS
CN Piperidine, 1-acetyl-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-4-methyl-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)



RN 666750-60-3 HCAPLUS
CN Morpholine, 4-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-4-methyl-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

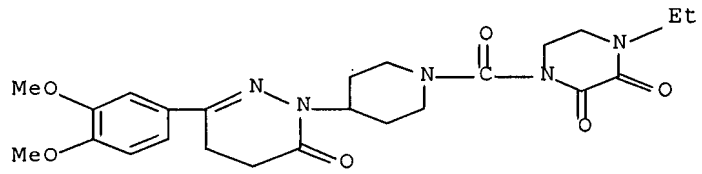


RN 666750-61-4 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-5-methyl-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

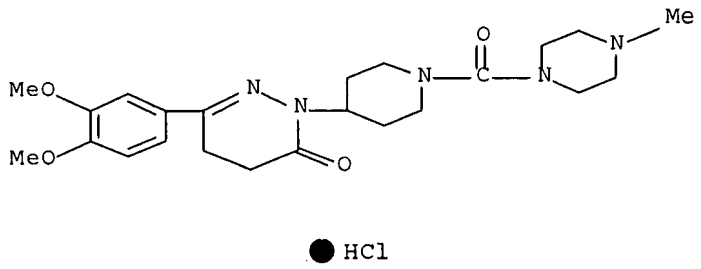


●2 HCl

RN 666750-62-5 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

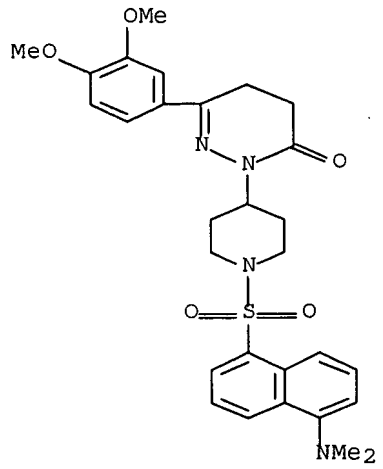


RN 666750-63-6 HCAPLUS
CN Piperazine, 1-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]carbonyl]-4-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

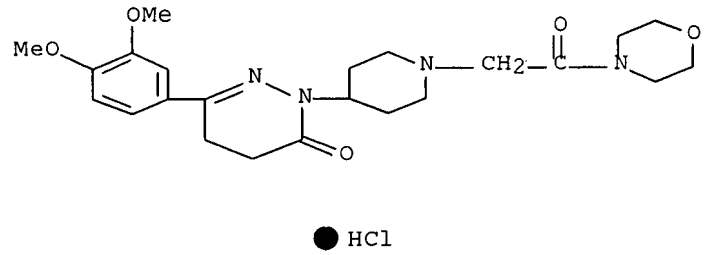


● HCl

RN 666750-64-7 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]- (9CI) (CA INDEX NAME)



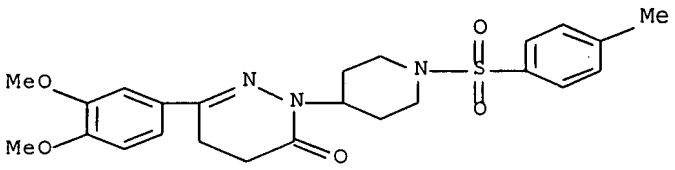
RN 666750-65-8 HCAPLUS
CN Morpholine, 4-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



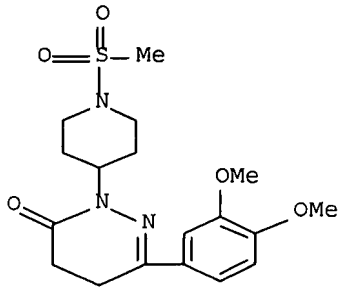
● HCl

RN 666750-66-9 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-

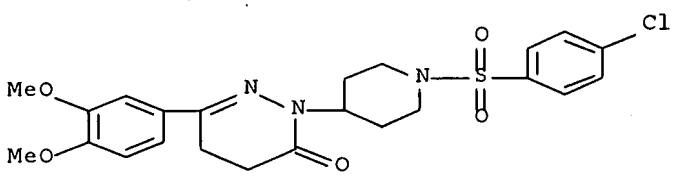
pyridazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



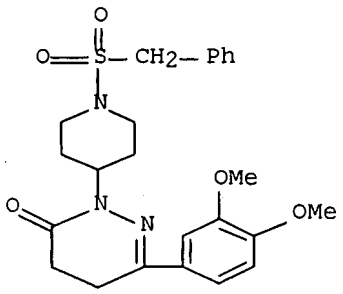
RN 666750-67-0 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)



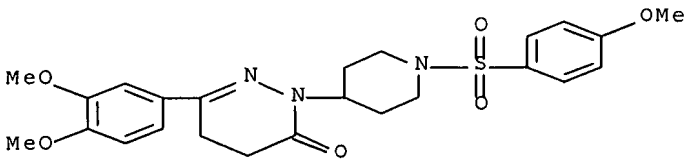
RN 666750-68-1 HCAPLUS
CN Piperidine, 1-[(4-chlorophenyl)sulfonyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)



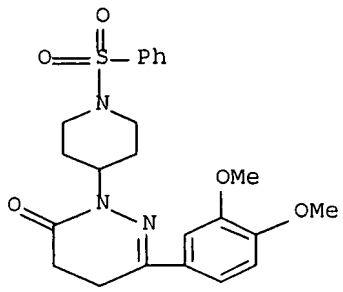
RN 666750-69-2 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[(phenylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)



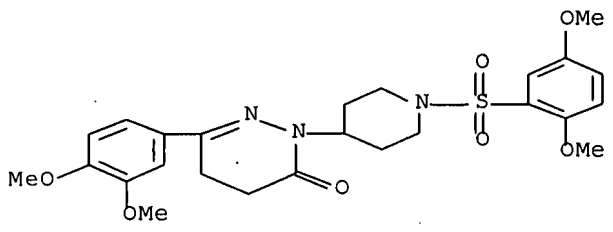
RN 666750-70-5 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[(4-methoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



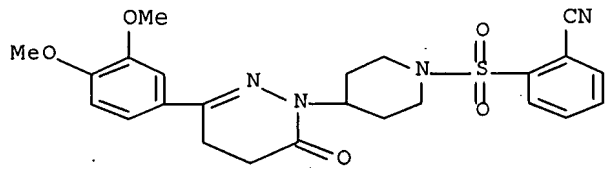
RN 666750-71-6 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-(phenylsulfonyl)- (9CI) (CA INDEX NAME)



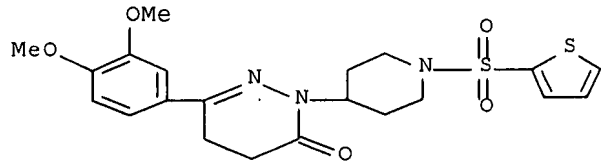
RN 666750-72-7 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)



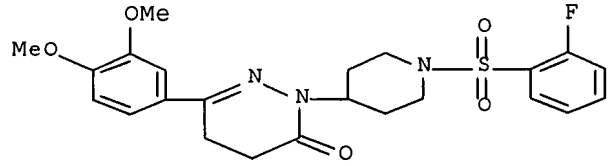
RN 666750-73-8 HCAPLUS
CN Piperidine, 1-[(2-cyanophenyl)sulfonyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)



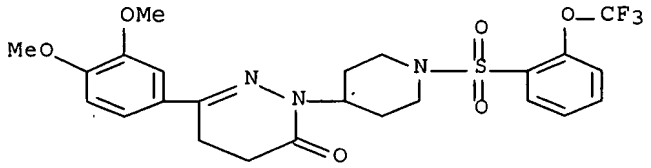
RN 666750-74-9 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)



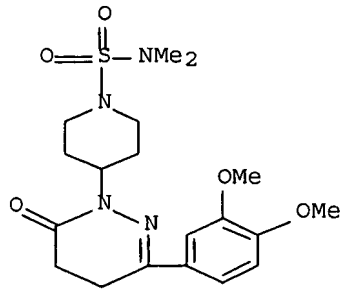
RN 666750-75-0 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)



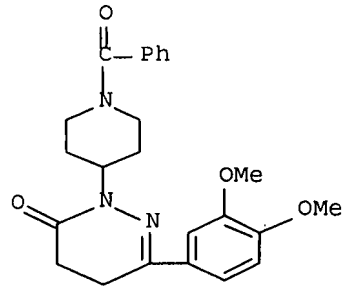
RN 666750-76-1 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[[2-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)



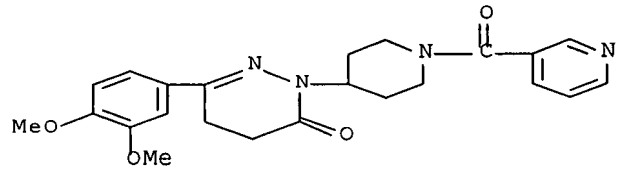
RN 666750-77-2 HCAPLUS
CN 1-Piperidinesulfonamide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-N,N-dimethyl- (CA INDEX NAME)



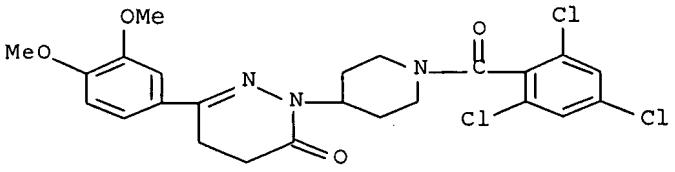
RN 666750-78-3 HCAPLUS
CN Piperidine, 1-benzoyl-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)



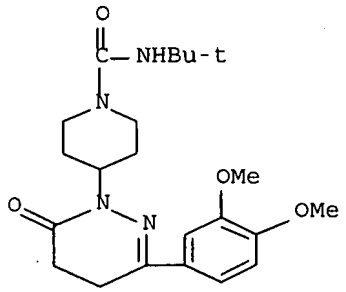
RN 666750-79-4 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-(3-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)



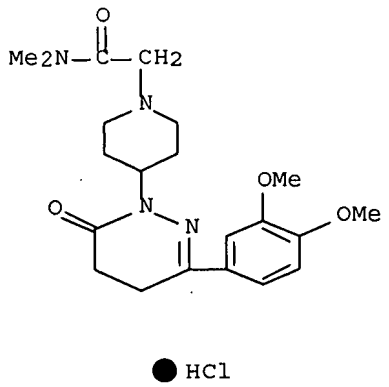
RN 666750-80-7 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-(2,4,6-trichlorobenzoyl)- (9CI) (CA INDEX NAME)



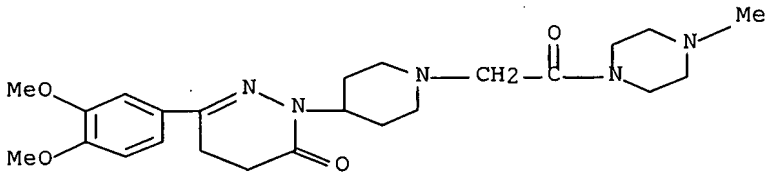
RN 666750-81-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)



RN 666750-82-9 HCAPLUS
CN 1-Piperidineacetamide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-N,N-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

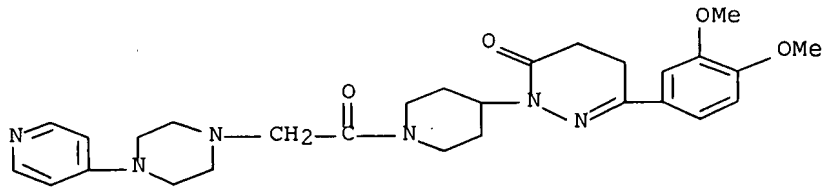


RN 666750-83-0 HCAPLUS
CN Piperazine, 1-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]acetyl]-4-methyl-, dihydrochloride (9CI) (CA INDEX NAME)



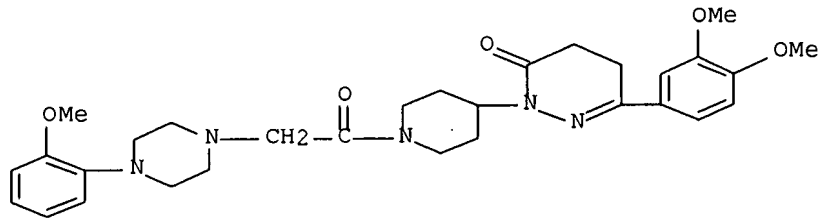
●2 HCl

RN 666750-84-1 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[[4-(4-pyridinyl)-1-piperazinyl]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



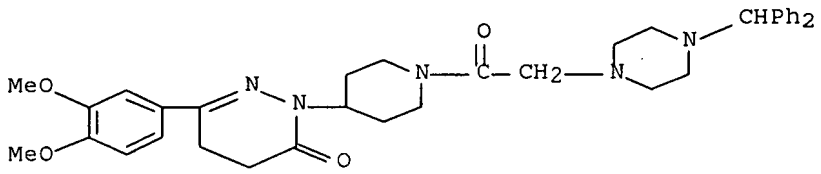
●2 HCl

RN 666750-85-2 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[[4-(2-methoxyphenyl)-1-piperazinyl]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



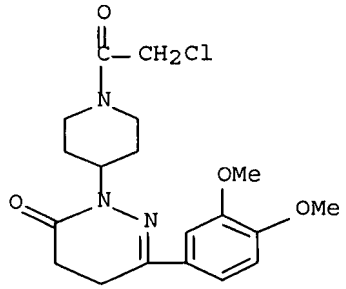
●2 HCl

RN 666750-86-3 HCAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[[4-(diphenylmethyl)-1-piperazinyl]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

IT **666750-88-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinylpyridazinones as phosphodiesterase PDE4 or PDE3/4 inhibitors)
RN 666750-88-5 HCAPLUS
CN Piperidine, 1-(chloroacetyl)-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)



IC ICM C07D401-04
ICS C07D401-14; A61K031-50
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**, **63**
IT **666750-56-7P**, 6-(3,4-Dimethoxyphenyl)-5-methyl-2-piperidin-4-yl-4,5-dihydro-2H-pyridazin-3-one hydrochloride **666750-57-8P** **666750-58-9P** **666750-59-0P** **666750-60-3P** **666750-61-4P** **666750-62-5P** **666750-63-6P** **666750-64-7P** **666750-65-8P** **666750-66-9P** **666750-67-0P** **666750-68-1P** **666750-69-2P** **666750-70-5P** **666750-71-6P** **666750-72-7P** **666750-73-8P** **666750-74-9P** **666750-75-0P** **666750-76-1P** **666750-77-2P** **666750-78-3P** **666750-79-4P** **666750-80-7P** **666750-81-8P** **666750-82-9P** **666750-83-0P** **666750-84-1P** **666750-85-2P** **666750-86-3P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinylpyridazinones as phosphodiesterase PDE4 or PDE3/4 inhibitors)

IT 380226-98-2P 380226-99-3P 380227-00-9P 666750-87-4P, 4-(7-Methoxy-2,2-dimethyl-2,3-dihydro-benzofuran-4-yl)-4-oxo-butyric acid **666750-88-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinylpyridazinones as phosphodiesterase PDE4 or PDE3/4 inhibitors)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182863 HCAPLUS Full-text
DOCUMENT NUMBER: 140:235730
TITLE: Preparation of piperidine-N-oxide derivatives as phosphodiesterase 4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Brundel, Paulus Johannes Gaurerius; Christiaans, Johannes A. M.; Menge, Wiro M. P. B.; Sterk, Geert Jan
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018450	A1	20040304	WO 2003-EP8676	20030806 <--
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2494643	A1	20040304	CA 2003-2494643	20030806 <--
AU 2003260371	A1	20040311	AU 2003-260371	20030806 <--
EP 1542987	A1	20050622	EP 2003-792258	20030806 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005538137	T	20051215	JP 2004-530087	20030806 <--
US 2006166995	A1	20060727	US 2005-523110	20050203 <--
PRIORITY APPLN. INFO.:			EP 2002-17978 A	20020810 <--
			WO 2003-EP8676 W	20030806 <--

OTHER SOURCE(S): MARPAT 140:235730
ED Entered STN: 05 Mar 2004
AB The 1,2-dihydro-2-(1-oxidopiperidin-4-yl)phthalazin-2-one derivs. [I; R1, R2 = H, C1-4 alkyl; or R1 and R2 together and with inclusion of the two carbon atoms, to which they are bonded, form a group selected from cyclohexane-1,2-diyl or 4-cyclohexene-1,2-diyl; R3 = a Ph derivative of formulas Q or Q1; R4 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; R5 = C1-8 alkoxy, C3-7 cycloalkoxy, C3-7 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R6 = C1-4

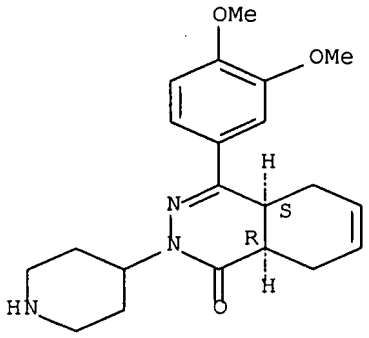
alkoxy, C3-5 cycloalkoxy, C3-5 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R7 = C1-4 alkyl; R8 = H, C1-4 alkyl; or wherein R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulfur atom; R9 = (CH2)mSO2R10, (CH2)nCOR11, -(CH2)p-Z-(CH2)q-R14; wherein R10, R11 = N(R12)R13; R12, R13 = H, C1-7 alkyl, C3-7 cycloalkyl, C3-7 cycloalkylmethyl; or NR12R13 together forms a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl- or a 1-hexahydroazepinyl ring; Z = a bond, O, CO, CONH, NHCO, SO2; R14 = H, OH, C1-4 alkoxy, hydroxy-C2-4 alkoxy, C1-4 alkoxy-C1-4 alkoxy, C1-4 alkoxycarbonyl, (un)substituted aminocarbonyl, etc.; m, n, p, q = an integer from 1 to 4] and the salts of these compds. are prepared These compds. are novel effective PDE4 inhibitors and useful for treating an illness treatable by the administration of a PDE4 inhibitor in a patient, in particular airway disorders. Thus, a solution of 1.2 g 2-[4-[(4aS,8aR)-4-(3,4-Dimethoxy)phenyl]-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]piperidin- 1-yl-2H-acetamide hydrochloride in 100 mL CH2Cl2 was washed with aqueous saturated NaHCO3 solution, dried over anhydrous MgSO4, cooled to 0°, treated with 0.6 g 3-chloroperbenzoic acid (70% purity), and stirred for 60 min to give, after workup and silica gel chromatog. and crystallization from EtOAc, 2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-1-oxypiperidin-1-yl]acetamide (II). II and 2-[4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H- phthalazin-2-yl]-1-oxypiperidin-1-yl]-N-isopropylacetamide showed -logIC50 (mol/L) of 8.31 and 9.3, resp., against PDE4.

IT **380226-97-1P 380227-13-4P**, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **449760-40-1P 449760-44-5P 666735-60-0P 666748-55-6P 666748-56-7P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating airway disorders)

RN 380226-97-1 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

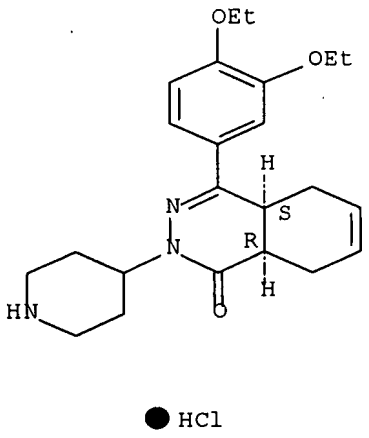
Absolute stereochemistry.



● HCl

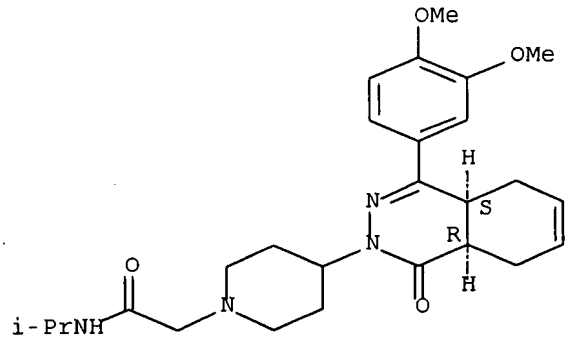
RN 380227-13-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



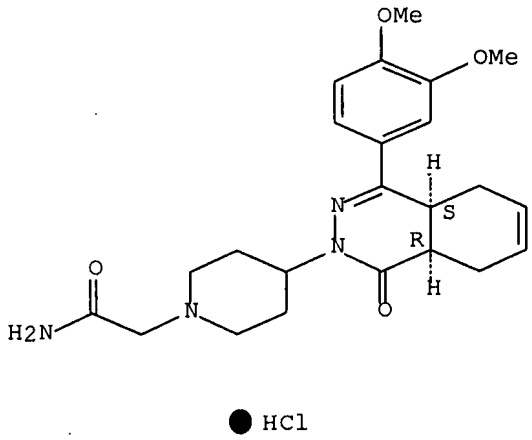
RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



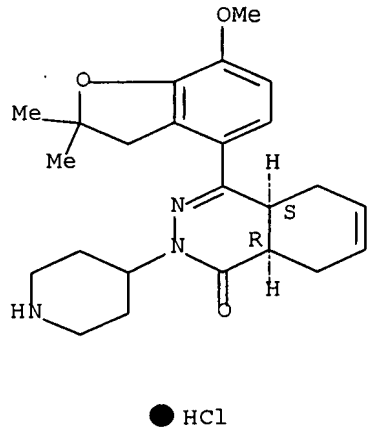
RN 449760-44-5 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



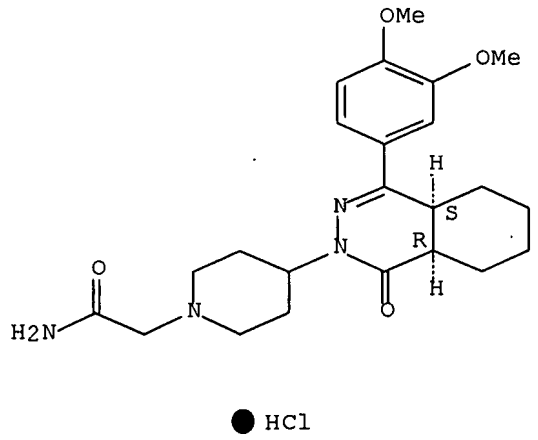
RN 666735-60-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



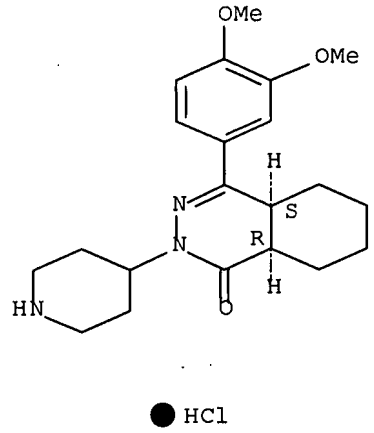
RN 666748-55-6 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



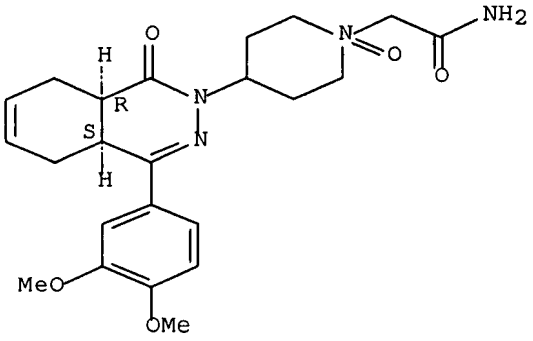
RN 666748-56-7 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



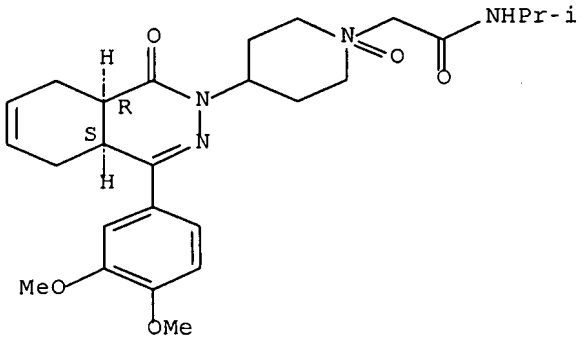
IT **666854-35-9P 666854-37-1P 666854-40-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating airway disorders)
RN 666854-35-9 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, 1-oxide (CA INDEX NAME)

Absolute stereochemistry.



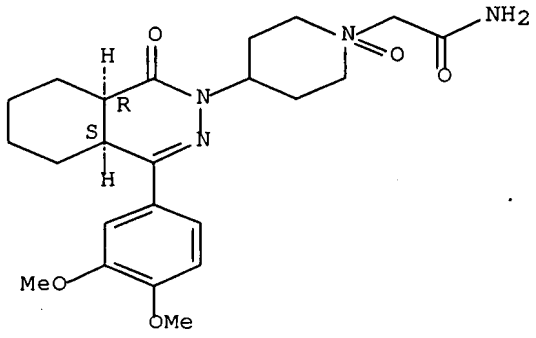
RN 666854-37-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)-, 1-oxide (CA INDEX NAME)

Absolute stereochemistry.



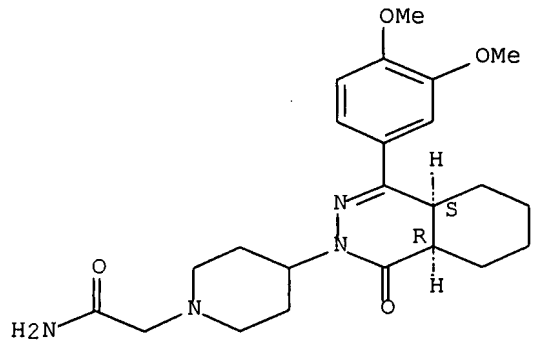
RN 666854-40-6 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-, 1-oxide (CA INDEX NAME)

Absolute stereochemistry.



IT **666748-54-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating airway disorders)
RN 666748-54-5 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



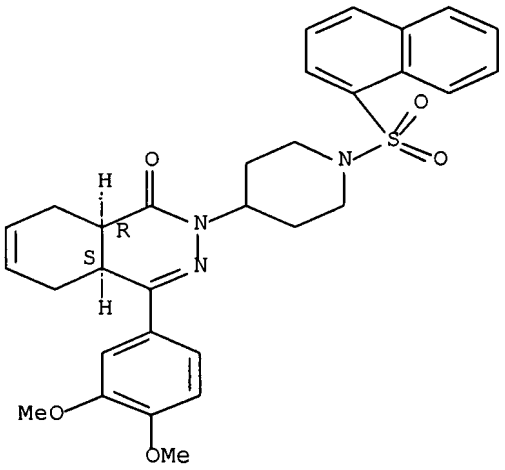
IC ICM C07D401-04
ICS C07D405-14; A61K031-50
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**, 7
IT 210467-67-7P 227967-42-2P, cis-2-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-carbonyl)-1,2,3,6-tetrahydrobenzoic acid 244077-33-6P, cis-2-(3,4-Diethoxybenzoyl)-1,2,3,6-tetrahydrobenzoic acid **380226-97-1P** 380226-98-2P, Piperidin-4-ylhydrazine dihydrochloride 380226-99-3P 380227-00-9P **380227-13-4P**, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **449760-40-1P 449760-44-5P 666735-60-0P 666748-55-6P 666748-56-7P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating airway disorders)
IT **666854-35-9P 666854-37-1P 666854-40-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating airway disorders)
IT 79-07-2, 2-Chloroacetamide 870-46-2, tert-Butyl carbazate 937-14-4, 3-Chloroperbenzoic acid 2627-86-3 79099-07-3, 4-Oxopiperidine-1-carboxylic acid tert-butyl ester 666735-58-6 666735-59-7 **666748-54-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating airway disorders)
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182862 HCAPLUS Full-text
DOCUMENT NUMBER: 140:217665
TITLE: Preparation of piperidinylphthalazinone derivatives as PDE4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christiaans, Johannes A. M.; Menge, Wiro M. P. B.; Sterk, Geert Jan; Weinbrenner, Steffen
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004018449	A1	20040304	WO 2003-EP8673	20030806 <--
WO 2004018449	A8	20040506		
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
AU 2003255376	A1	20040311	AU 2003-255376	20030806 <--
PRIORITY APPLN. INFO.:			EP 2002-17979 A	20020810 <--
			WO 2003-EP8673 W	20030806 <--

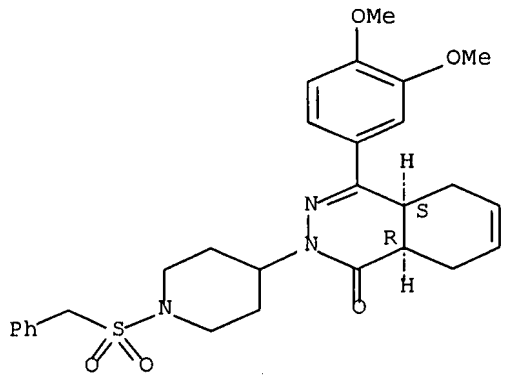
OTHER SOURCE(S): MARPAT 140:217665
ED Entered STN: 05 Mar 2004
AB The title compound I [R1, R2 = H or together form an addnl. bond; R3 = benzene derivative Q1 or Q2; R4 = (substituted)arylsulfonyl; R5 = alkoxy or polyfluoroalkyoxy; R6, R7 = (cyclo)alkoxy, cycloalkylmethoxy, or polyfluoroalkyoxy; R8 = alkyl; R9 = H or alkyl; or R7 and R8 together with the 2 intervening C atoms form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by O or S] were prepared as PDE4 inhibitors. Thus, reaction of (4aS,8aR)-4-(3,4-dimethoxyphenyl)-2- piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (preparation given) with naphthalene-1-sulfonyl chloride gave compound II. The prepared compds. inhibited PDE4 with -log(IC50) ≥ 8.8.
IT **666737-07-1P 666737-09-3P 666737-10-6P**
666737-11-7P 666737-12-8P 666737-13-9P
666737-14-0P 666737-15-1P 666737-16-2P
666737-17-3P 666737-18-4P 666737-19-5P
666737-20-8P 666737-21-9P 666737-22-0P
666737-23-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinylphthalazinone derivs. as PDE4 inhibitors)
RN 666737-07-1 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



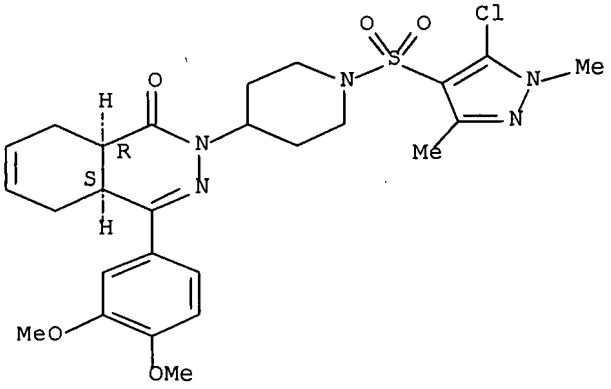
RN 666737-09-3 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(phenylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



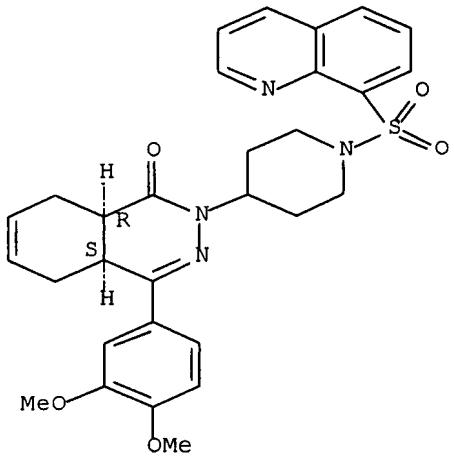
RN 666737-10-6 HCAPLUS
CN Piperidine, 1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



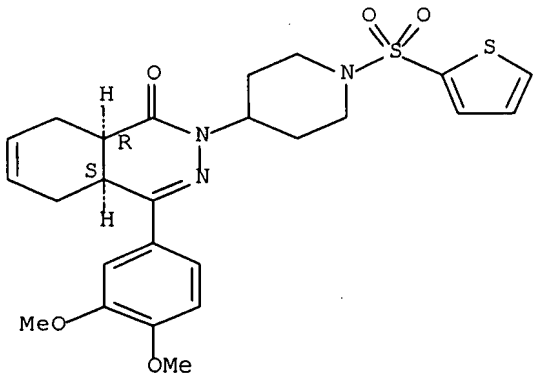
RN 666737-11-7 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(8-quinolinylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



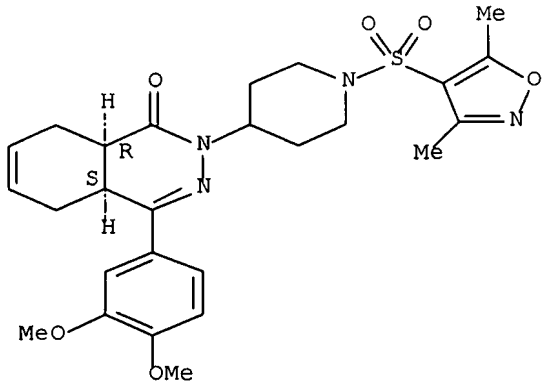
RN 666737-12-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



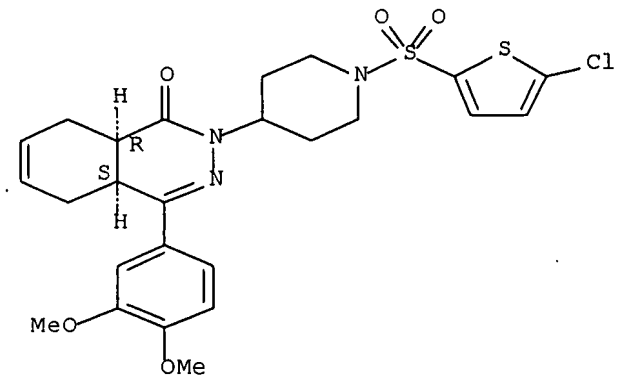
RN 666737-13-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(3,5-dimethyl-4-isoxazolyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



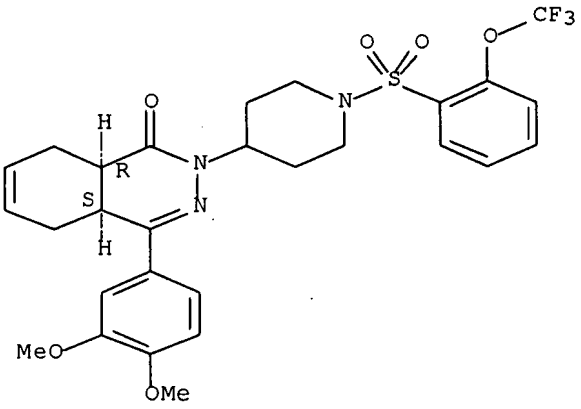
RN 666737-14-0 HCAPLUS
CN Piperidine, 1-[(5-chloro-2-thienyl)sulfonyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



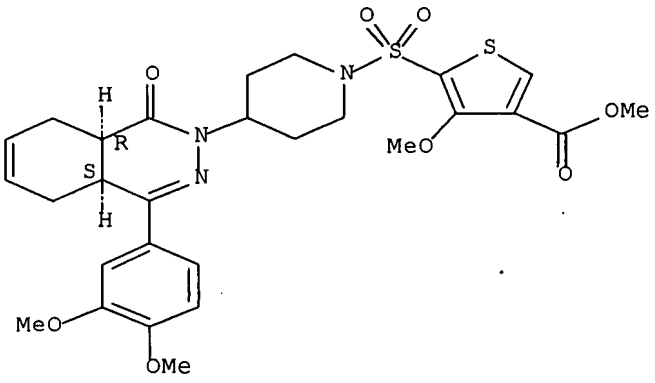
RN 666737-15-1 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[2-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



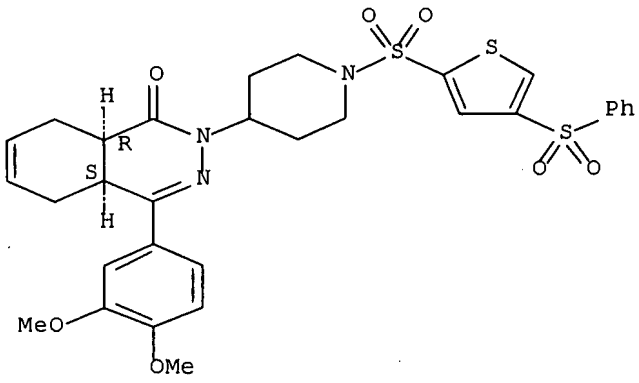
RN 666737-16-2 HCAPLUS
CN 3-Thiophenecarboxylic acid, 5-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]sulfonyl]-4-methoxy-, methyl ester (CA INDEX NAME)

Absolute stereochemistry.



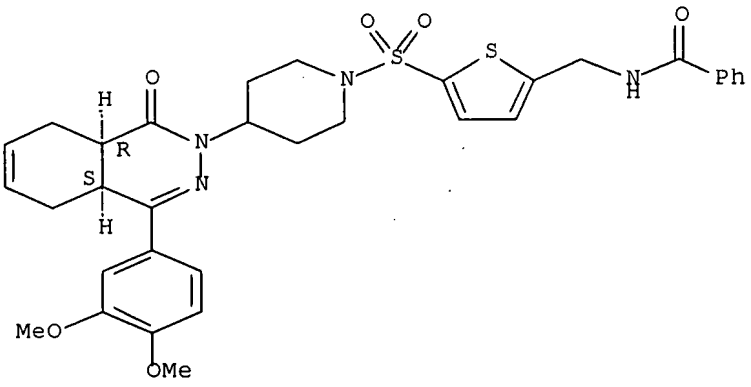
RN 666737-17-3 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[4-(phenylsulfonyl)-2-thienyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



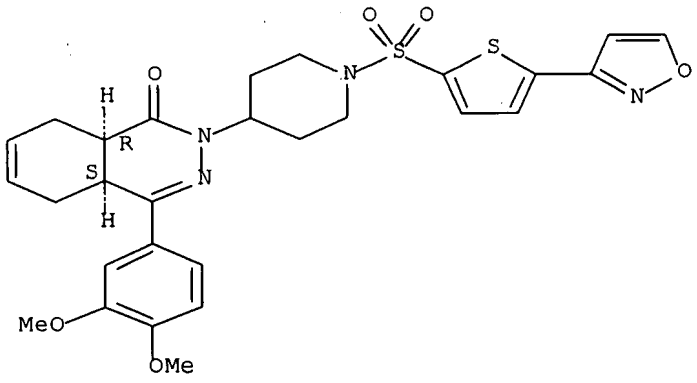
RN 666737-18-4 HCAPLUS
CN Benzamide, N-[[5-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]sulfonyl]-2-thienyl]methyl]- (CA INDEX NAME)

Absolute stereochemistry.



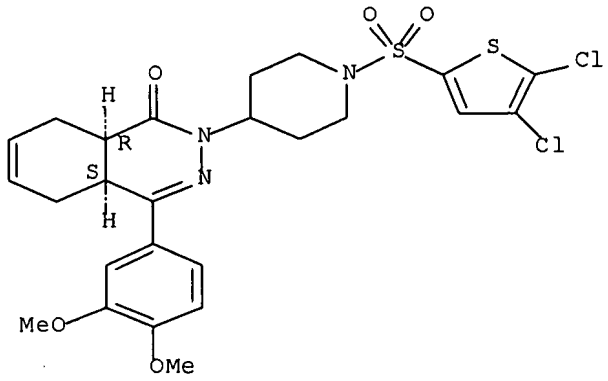
RN 666737-19-5 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(3-isoxazolyl)-2-thienyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



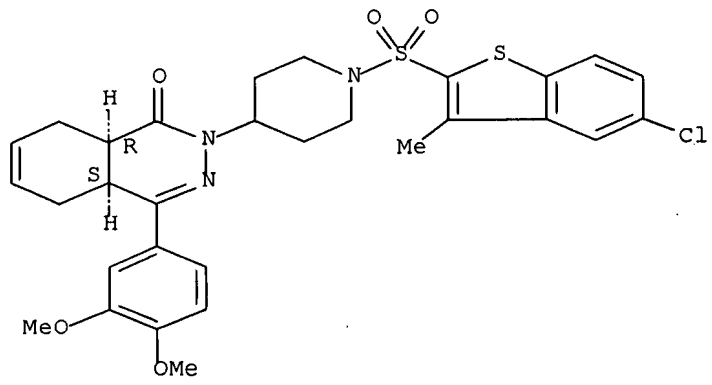
RN 666737-20-8 HCAPLUS
CN Piperidine, 1-[(4,5-dichloro-2-thienyl)sulfonyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



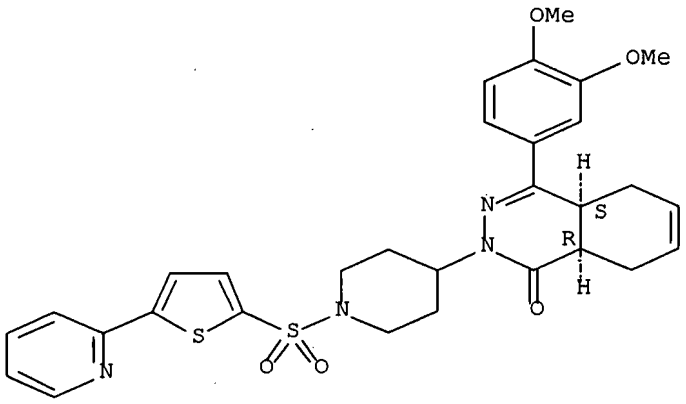
RN 666737-21-9 HCAPLUS
CN Piperidine, 1-[(5-chloro-3-methylbenzo[b]thien-2-yl)sulfonyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



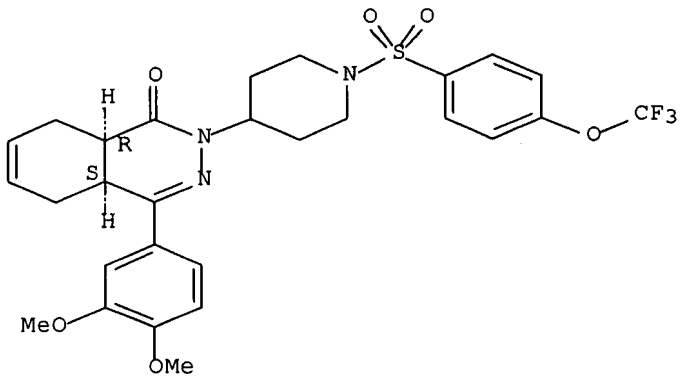
RN 666737-22-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



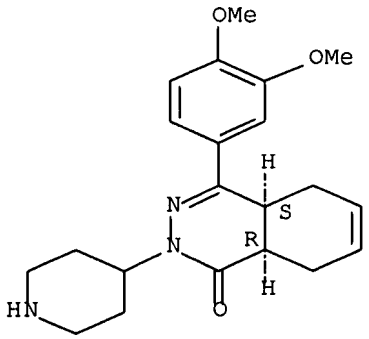
RN 666737-23-1 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **380226-97-1P 380227-13-4P 666735-60-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinylphthalazinone derivs. as PDE4 inhibitors)
RN 380226-97-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

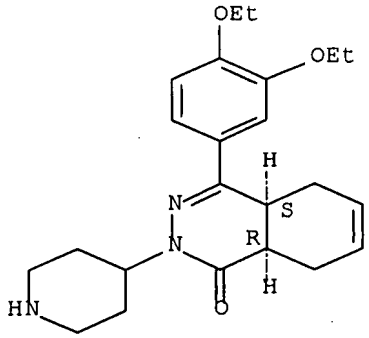
Absolute stereochemistry.



● HCl

RN 380227-13-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

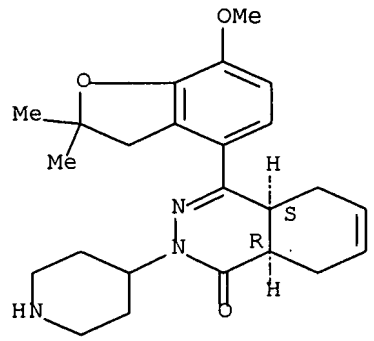
Absolute stereochemistry.



● HCl

RN 666735-60-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

IC ICM C07D401-04
ICS C07D401-14; C07D409-14; C07D413-14; A61K031-50; A61P029-00
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**, 27, **63**
IT **666737-07-1P 666737-09-3P 666737-10-6P**
666737-11-7P 666737-12-8P 666737-13-9P
666737-14-0P 666737-15-1P 666737-16-2P
666737-17-3P 666737-18-4P 666737-19-5P
666737-20-8P 666737-21-9P 666737-22-0P
666737-23-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinylphthalazinone derivs. as PDE4 inhibitors)
IT **380226-97-1P** 380226-98-2P 380226-99-3P **380227-13-4P**
666735-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinylphthalazinone derivs. as PDE4 inhibitors)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:182711 HCAPLUS Full-text
DOCUMENT NUMBER: 140:235729
TITLE: Preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors
INVENTOR(S): Sterk, Geert Jan; Hatzelmann, Armin; Marx, Degenhard; Kley, Hans-Peter; Menge, Wiro M. P. B.
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

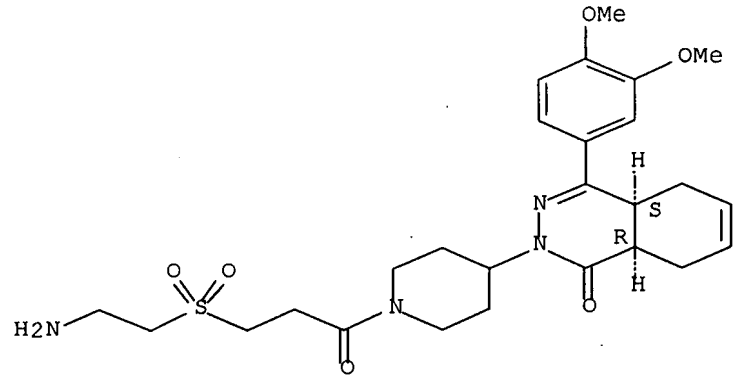
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004017974	A1	20040304	WO 2003-EP8724	20030806 <--
W: AE, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GE, HR, ID, IL, IN, IS,				

JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2494634	A1	20040304	CA 2003-2494634	20030806 <--
AU 2003260376	A1	20040311	AU 2003-260376	20030806 <--
EP 1556049	A1	20050727	EP 2003-792267	20030806 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005538140	T	20051215	JP 2004-530096	20030806 <--
AT 360627	T	20070515	AT 2003-792257	20030806 <--
US 2006094710	A1	20060504	US 2005-523111	20051003 <--
PRIORITY APPLN. INFO.:			EP 2002-17977 A	20020810 <--
			WO 2003-EP8724 W	20030806 <--

OTHER SOURCE(S): MARPAT 140:235729
ED Entered STN: 05 Mar 2004
AB Title compds. I [R1-2 = H, alkyl, etc.; R3 = substituted Ph, etc.; R9 = naphthyl, pyrazinyl, pyridazinyl, etc.] are prepared For instance, (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H- phthalazin-1-one hydrochloride (preparation given) is reacted with methanesulfonylacetic acid (CH2Cl2, Et3N) to give II. Compds. of the invention have pIC50 ≥ 9 for the PDE4 receptor. I are useful for the treatment of airway disorders.
IT **666851-01-0P**, (4AS,8aR)-2-[1-[3-(2-aminoethanesulfonyl)propanoyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors)
RN 666851-01-0 HCAPLUS
CN Piperidine, 1-[3-[(2-aminoethyl)sulfonyl]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

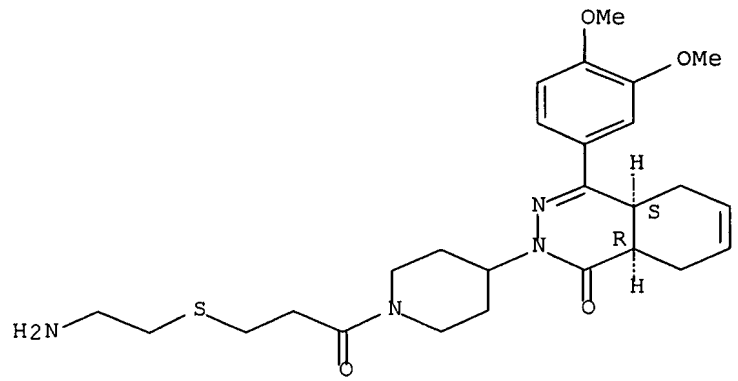


IT **380227-17-8P**, (4AS,8aR)-2-[1-[3-[(2-Aminoethyl)sulfanyl]propanoyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666850-88-0P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[[2-(methanesulfonyl)ethane]carbonyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666850-90-4P**, (4AS,8aR)-2-[1-[2-(Benzofuran-2-

yl)-2-oxoethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666850-93-7P**, (4AS,8aR)-2-[1-[4-(Benzimidazol-1-yl)benzyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666850-96-0P 666850-99-3P 666851-03-2P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[2-[(2-oxo-1,2-dihydroquinolin-6-yl)oxy]ethanoyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666851-05-4P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[4-[(2-oxo-1,2-dihydroquinolin-6-yl)oxy]butanoyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666851-07-6P**, (4AS,8aR)-2-[1-[2-(2-Aminoethoxy)ethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one dihydrochloride **666851-10-1P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-methoxyethyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666851-12-3P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-methylsulfanylethyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666851-15-6P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[2-(methanesulfonyl)ethyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666851-17-8P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[2-(2-hydroxyethoxy)ethyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666851-19-0P**, 6-[4-[4-[3-(3,4-Dimethoxyphenyl)-6-oxo-5,6-dihydro-4H-pyridazin-1-yl]piperidin-1-yl]-4-oxobutoxy]-1H-quinolin-2-one **666851-37-2P**, (4AS,8aR)-2-[1-[2-(2-Aminoethoxy)ethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors)

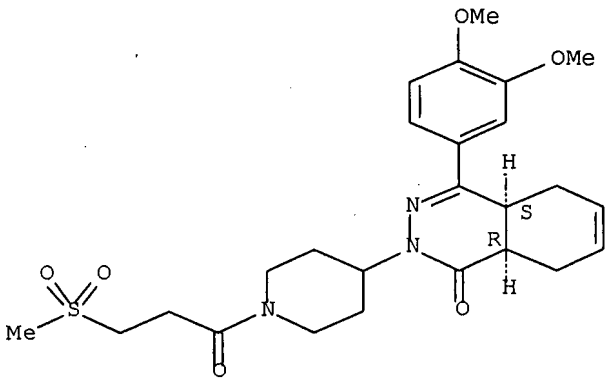
RN 380227-17-8 HCAPLUS
CN Piperidine, 1-[3-[(2-aminoethyl)thio]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



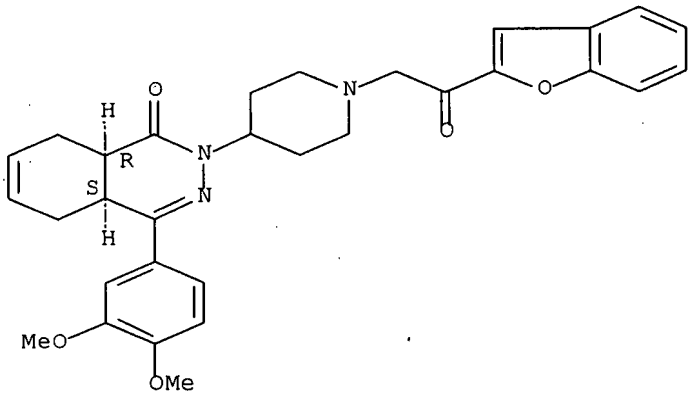
RN 666850-88-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[3-(methylsulfonyl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



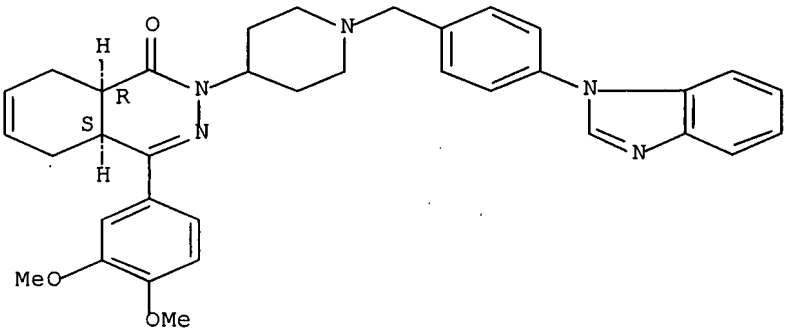
RN 666850-90-4 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(2-benzofuranyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 666850-93-7 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[[4-(1H-benzimidazol-1-yl)phenyl]methyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

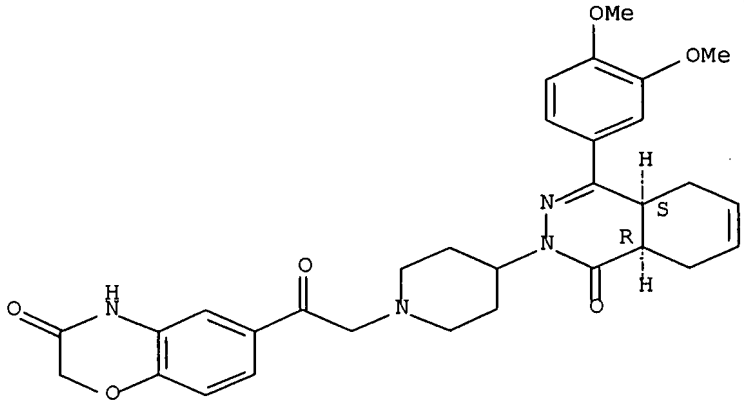
Absolute stereochemistry.



● HCl

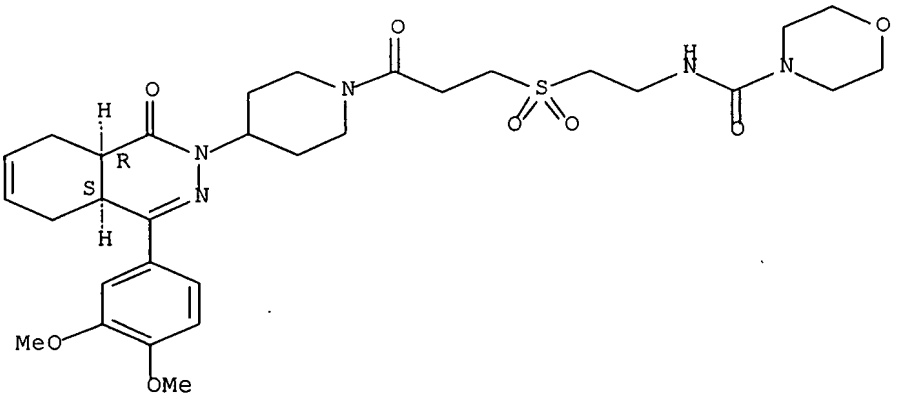
RN 666850-96-0 HCAPLUS
CN 2H-1,4-Benzoxazin-3(4H)-one, 6-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



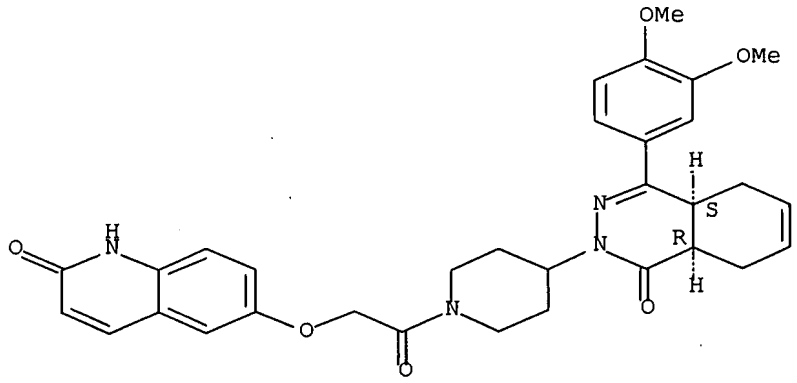
RN 666850-99-3 HCAPLUS
CN 4-Morpholinecarboxamide, N-[2-[[3-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-3-oxopropyl]sulfonyl]ethyl]- (CA INDEX NAME)

Absolute stereochemistry.



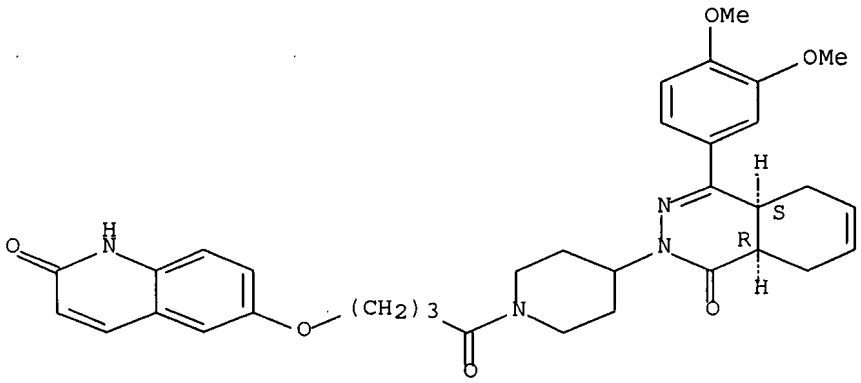
RN 666851-03-2 HCAPLUS
CN Piperidine, 1-[[(1,2-dihydro-2-oxo-6-quinolinyl)oxy]acetyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



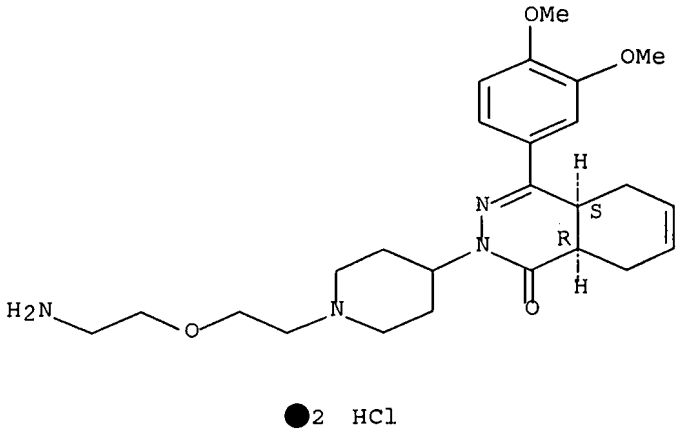
RN 666851-05-4 HCAPLUS
CN Piperidine, 1-[4-[(1,2-dihydro-2-oxo-6-quinolinyl)oxy]-1-oxobutyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



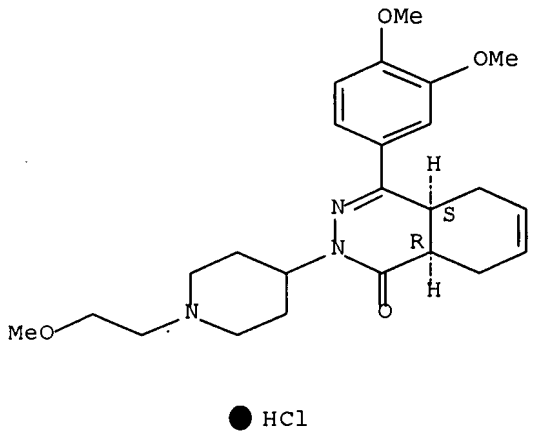
RN 666851-07-6 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(2-aminoethoxy)ethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, dihydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



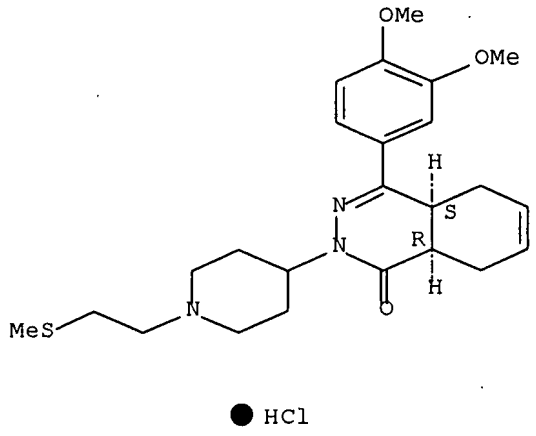
RN 666851-10-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-methoxyethyl)-4-piperidinyl]-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



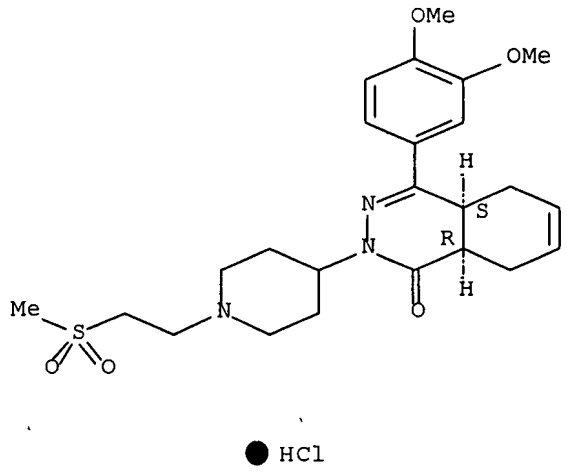
RN 666851-12-3 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[2-(methylthio)ethyl]-4-piperidinyl]-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



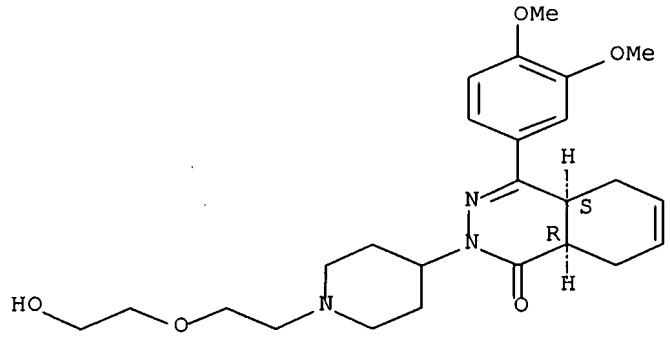
RN 666851-15-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[2-(methylsulfonyl)ethyl]-4-piperidinyl]-, monohydrochloride, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

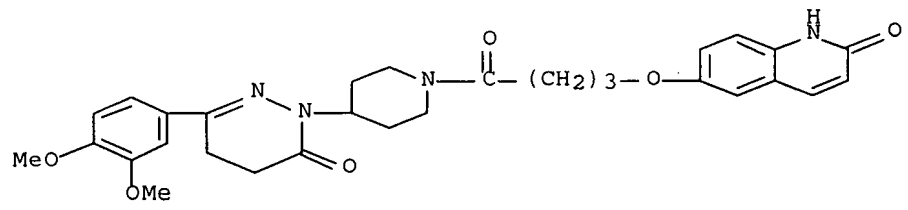


RN 666851-17-8 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[2-(2-hydroxyethoxy)ethyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



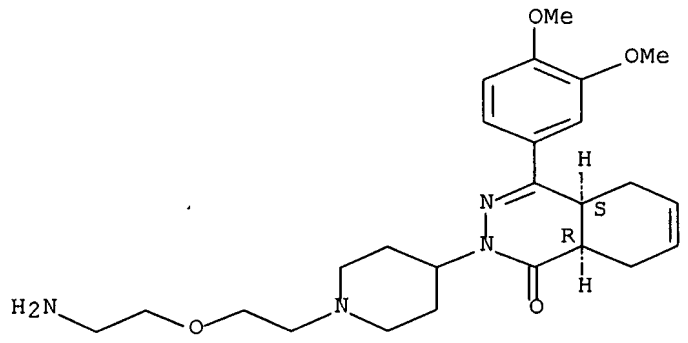
RN 666851-19-0 HCAPLUS
CN Piperidine, 1-[4-[(1,2-dihydro-2-oxo-6-quinolinyl)oxy]-1-oxobutyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)



RN 666851-37-2 HCAPLUS

CN 1(2H)-Phthalazinone, 2-[1-[2-(2-aminoethoxy)ethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

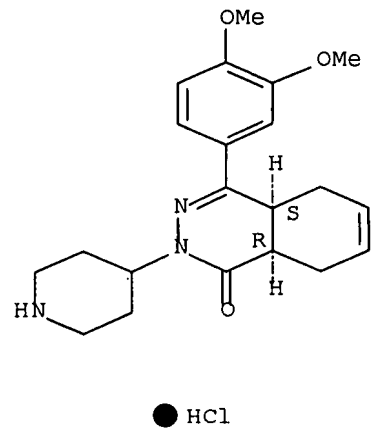


IT **380226-97-1P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **380227-13-4P**, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666735-60-0P 666750-56-7P**, 6-(3,4-Dimethoxyphenyl)-5-methyl-2-(piperidin-4-yl)-4,5-dihydro-2H-pyridazin-3-one hydrochloride **666750-57-8P**, 6-(3,4-Dimethoxyphenyl)-2-(piperidin-4-yl)-4,5-dihydro-2H-pyridazin-3-one hydrochloride **666750-58-9P**, 6-(7-Methoxy-2,2-dimethyl-2,3-dihydrobenzofuran-4-yl)-2-(piperidin-4-yl)-4,5-dihydro-2H-pyridazin-3-one hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors)

RN 380226-97-1 HCAPLUS

CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

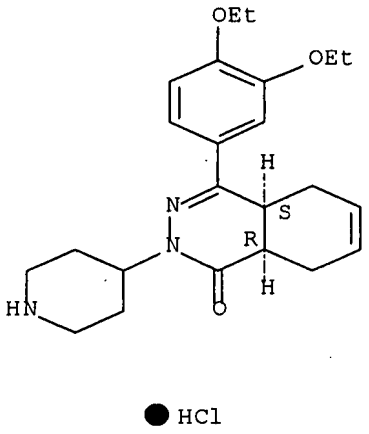
Absolute stereochemistry.



● HCl

RN 380227-13-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

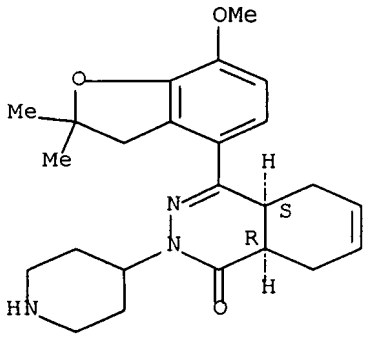
Absolute stereochemistry.



● HCl

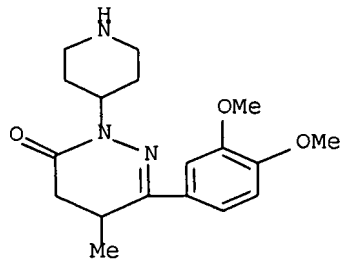
RN 666735-60-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



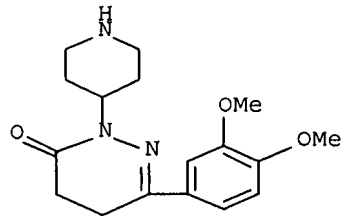
● HCl

RN 666750-56-7 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-5-methyl-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



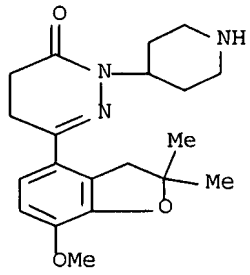
● HCl

RN 666750-57-8 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 666750-58-9 HCAPLUS
CN 3(2H)-Pyridazinone, 6-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IC ICM A61K031-502
ICS A61K031-50; C07D401-04; C07D401-14; C07D405-14; A61P011-00
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): **1**, **63**

IT **666851-01-0P**, (4AS,8aR)-2-[1-[3-(2-aminoethanesulfonyl)propanoyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors)

IT **380227-17-8P**, (4AS,8aR)-2-[1-[3-[(2-Aminoethyl)sulfanyl]propanoyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666850-88-0P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[[2-(methanesulfonyl)ethane]carbonyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666850-90-4P**, (4AS,8aR)-2-[1-[2-(Benzofuran-2-yl)-2-oxoethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666850-93-7P**, (4AS,8aR)-2-[1-[4-(Benzimidazol-1-yl)benzyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666850-96-0P 666850-99-3P 666851-03-2P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[2-[(2-oxo-1,2-dihydroquinolin-6-yl)oxy]ethanoyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666851-05-4P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[4-[(2-oxo-1,2-dihydroquinolin-6-yl)oxy]butanoyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666851-07-6P**, (4AS,8aR)-2-[1-[2-(2-Aminoethoxy)ethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one dihydrochloride **666851-10-1P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-methoxyethyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666851-12-3P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-methylsulfanylethyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666851-15-6P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[2-(methanesulfonyl)ethyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666851-17-8P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[2-(2-hydroxyethoxy)ethyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one **666851-19-0P**, 6-[4-[4-[3-(3,4-Dimethoxyphenyl)-6-oxo-5,6-dihydro-4H-pyridazin-1-yl]piperidin-1-yl]-4-oxobutoxy]-1H-quinolin-2-one **666851-37-2P**, (4AS,8aR)-2-[1-[2-(2-Aminoethoxy)ethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors)

IT **380226-97-1P**, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride 380226-98-2P, (Piperidin-4-yl)hydrazine dihydrochloride 380226-99-3P 380227-00-9P **380227-13-4P**, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride **666735-60-0P 666750-56-7P**, 6-(3,4-Dimethoxyphenyl)-5-methyl-2-(piperidin-4-yl)-4,5-dihydro-2H-pyridazin-3-one hydrochloride **666750-57-8P**, 6-(3,4-Dimethoxyphenyl)-2-(piperidin-4-yl)-4,5-dihydro-2H-pyridazin-3-one hydrochloride **666750-58-9P**, 6-(7-Methoxy-2,2-dimethyl-2,3-dihydrobenzofuran-4-yl)-2-(piperidin-4-yl)-4,5-dihydro-2H-pyridazin-3-one hydrochloride 666750-87-4P, 4-(7-Methoxy-2,2-dimethyl-2,3-dihydrobenzofuran-4-yl)-4-oxobutanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidine-substituted pyridazones and phthalazones as PDE4 inhibitors)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:719308 HCAPLUS Full-text
DOCUMENT NUMBER: 139:240373
TITLE: Pharmaceutical composition of a phosphodiesterase 4 (PDE4) inhibitor or a PDE3/4 inhibitor and a histamine receptor antagonist for the treatment of respiratory diseases
INVENTOR(S): Beume, Rolf; Bundschuh, Daniela; Weimar, Christian; Wollin, Stefan-lutz
PATENT ASSIGNEE(S): Altana Pharma Ag, Germany
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074055	A1	20030912	WO 2003-EP1876	20030225 <--
W: AE, AL, AU, BA, BR, CA, CN, CO, CU, DZ, EC, GE, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZW				
RW: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR				
CA 2478612	A1	20030912	CA 2003-2478612	20030225 <--
AU 2003212268	A1	20030916	AU 2003-212268	20030225 <--
EP 1482938	A1	20041208	EP 2003-708130	20030225 <--
EP 1482938	B1	20070808		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003008220	A	20050104	BR 2003-8220	20030225 <--
JP 2005524666	T	20050818	JP 2003-572572	20030225 <--
NZ 535611	A	20060331	NZ 2003-535611	20030225 <--
AT 369134	T	20070815	AT 2003-708130	20030225 <--
IN 2004MN00404	A	20050218	IN 2004-MN404	20040723 <--
MX 2004PA08460	A	20041206	MX 2004-PA8460	20040901 <--
US 2005112069	A1	20050526	US 2004-506875	20040903 <--
NO 2004004230	A	20041206	NO 2004-4230	20041006 <--
PRIORITY APPLN. INFO.:			EP 2002-4987 A	20020306 <--
			WO 2003-EP1876 W	20030225 <--

ED Entered STN: 14 Sep 2003
AB The invention discloses the combined administration of PDE4 or PDE3/4 inhibitors and histamine receptor antagonists for the treatment of respiratory diseases.
IT **449760-14-9 449760-15-0 449760-16-1**
449760-17-2 449760-19-4 449760-20-7
449760-22-9 449760-23-0 449760-24-1
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449760-29-6 449760-30-9 449760-35-4
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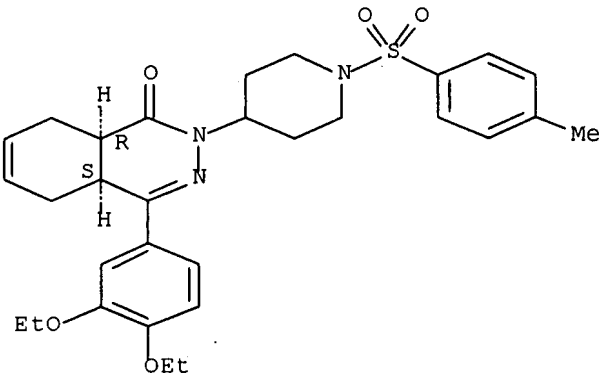
449760-51-4 449760-52-5 449760-53-6
449760-56-9 449760-57-0 449760-58-1
596102-01-1 596102-07-7 596102-09-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)
(phosphodiesterase 4 (PDE4) inhibitor or PDE3/4 inhibitor combination with histamine receptor antagonist for treatment of respiratory disease)

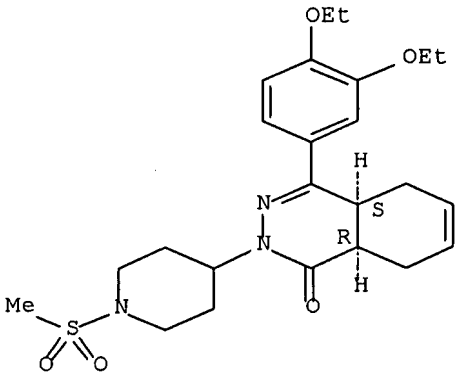
RN 449760-14-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



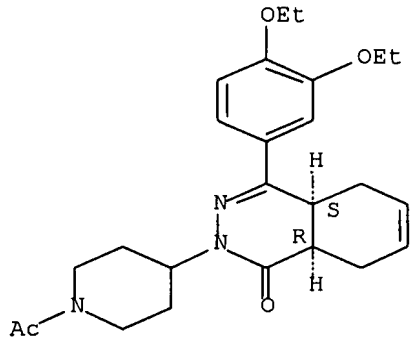
RN 449760-15-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



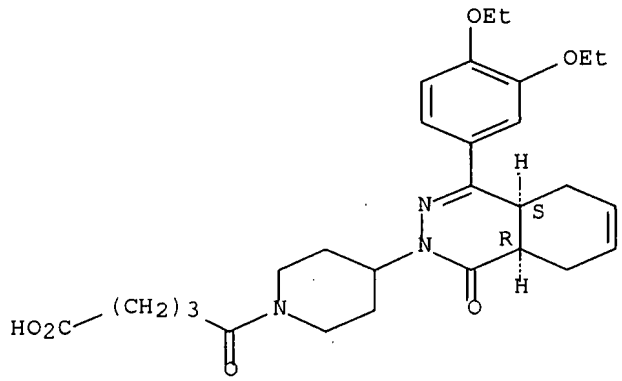
RN 449760-16-1 HCAPLUS
CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



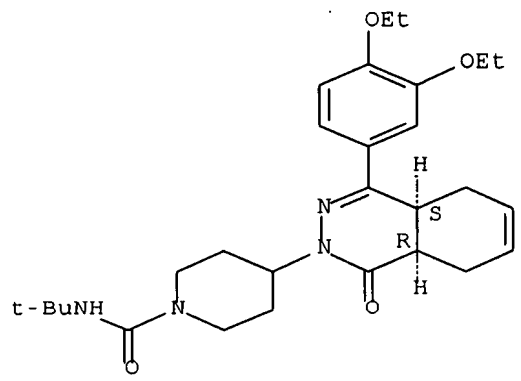
RN 449760-17-2 HCAPLUS
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



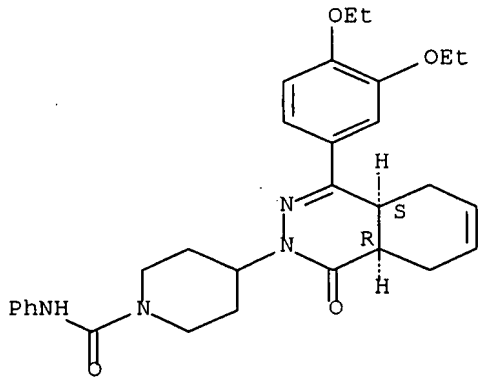
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



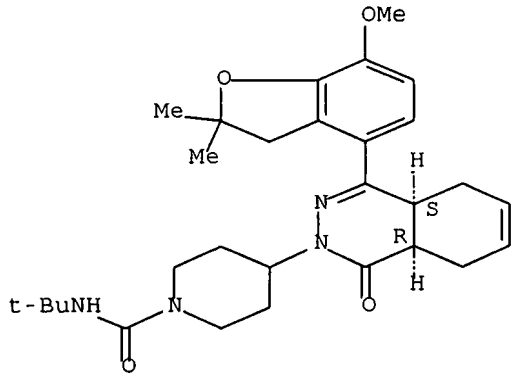
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

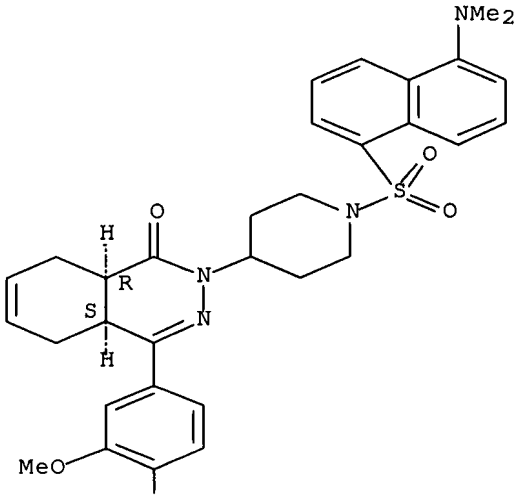
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

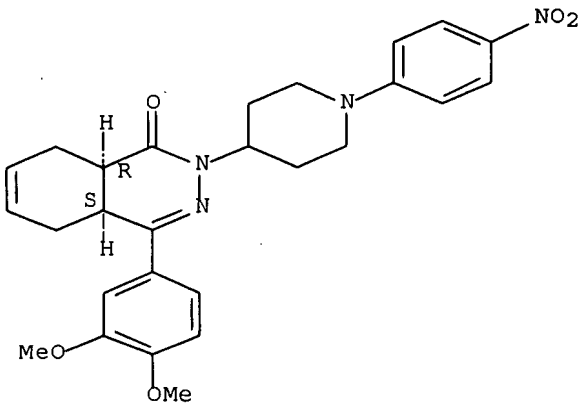
PAGE 1-A



PAGE 2-A

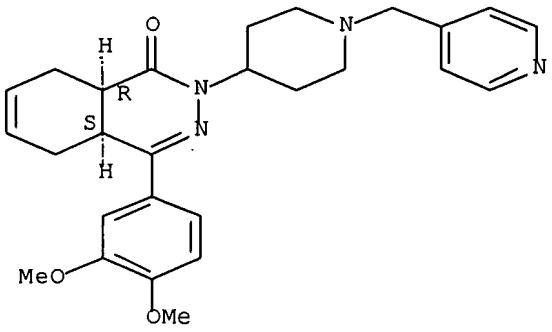
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



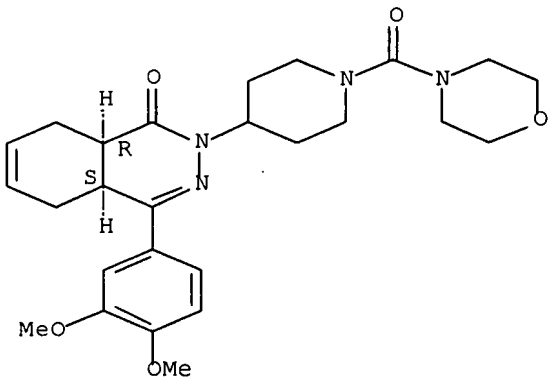
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



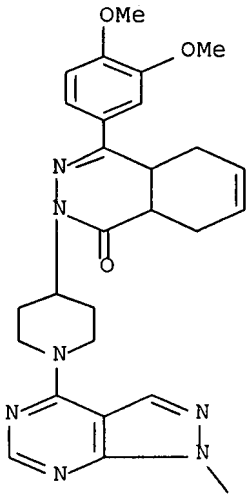
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A



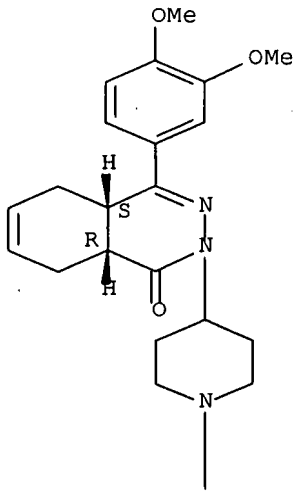
PAGE 2-A

Me

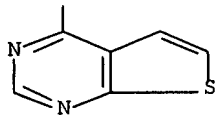
RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

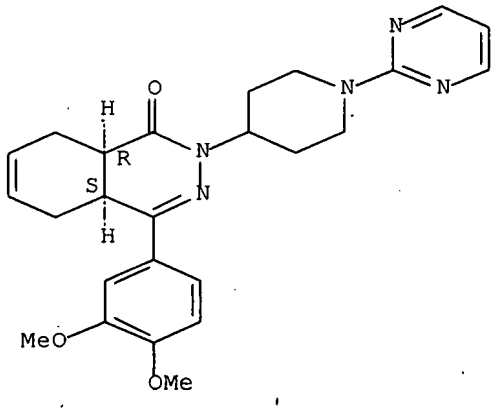


PAGE 2-A



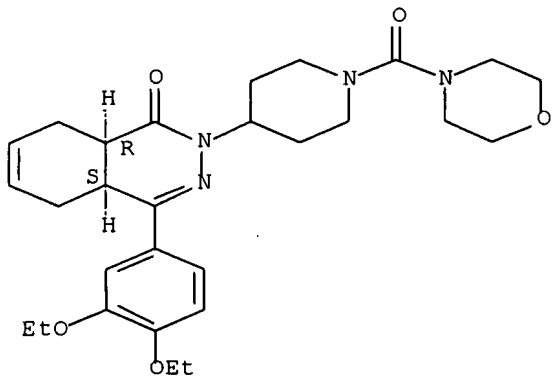
RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

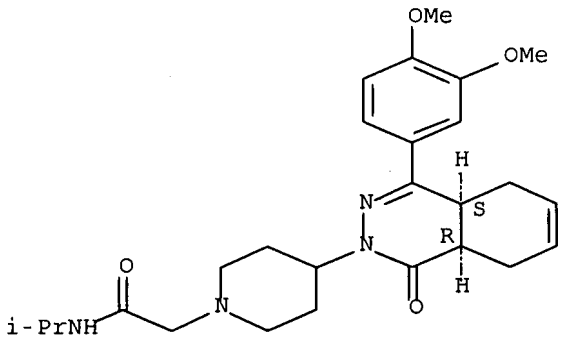
Absolute stereochemistry.



RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-

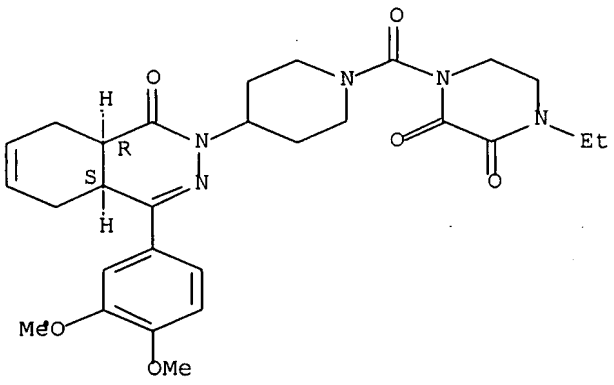
tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



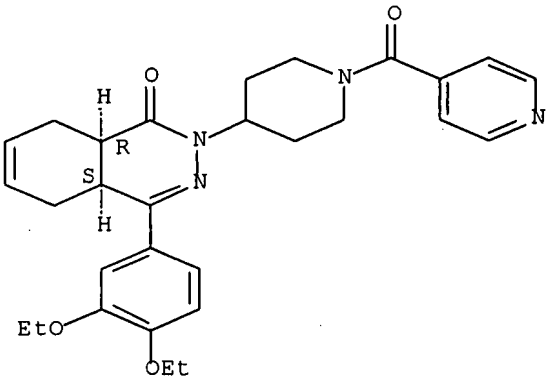
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



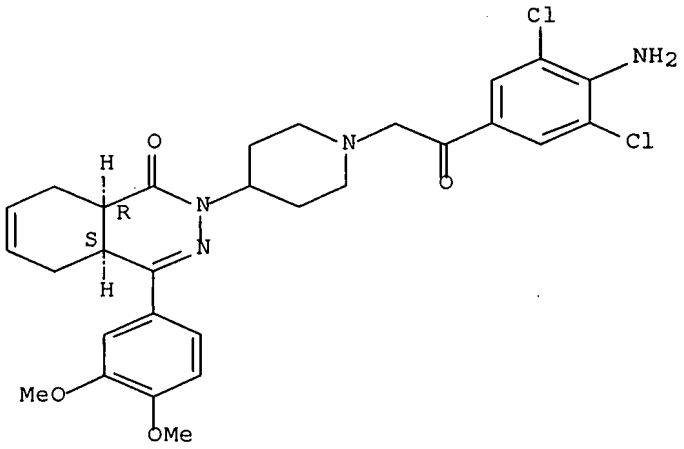
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



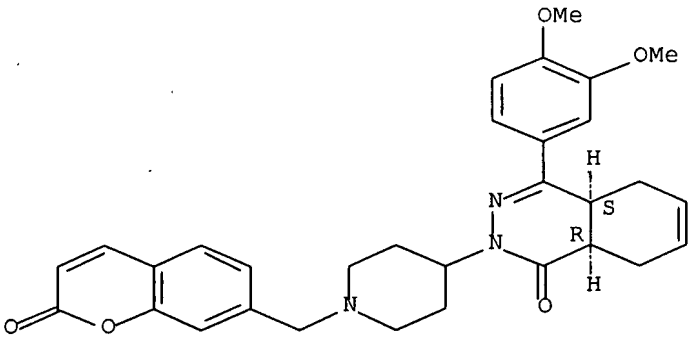
RN 449760-48-9 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



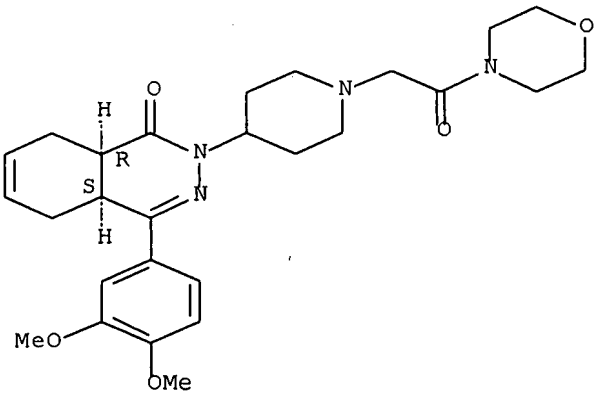
RN 449760-49-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



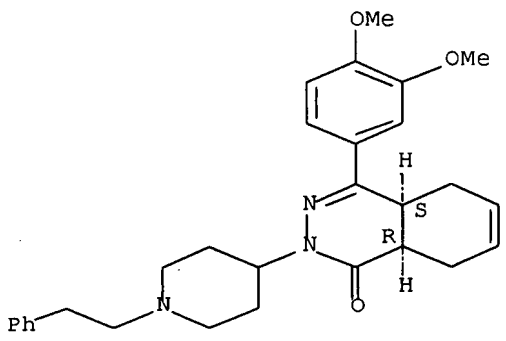
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



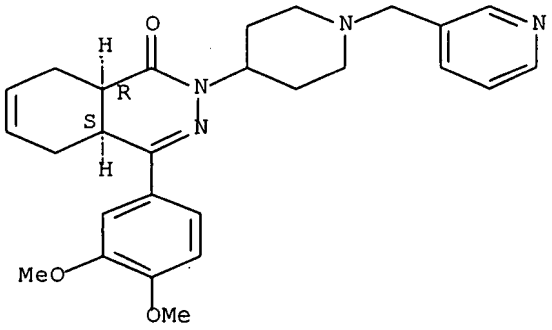
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



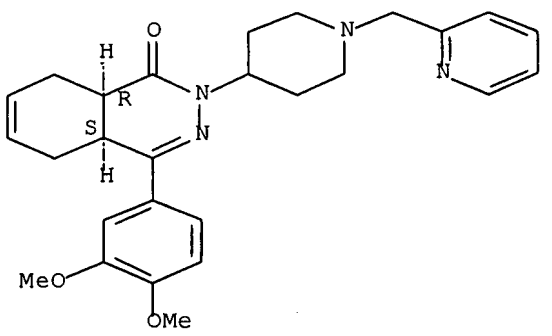
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



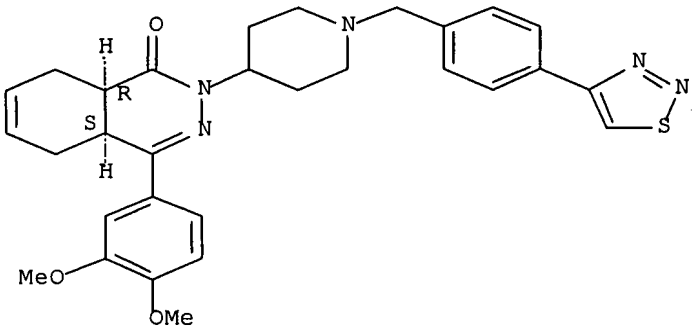
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



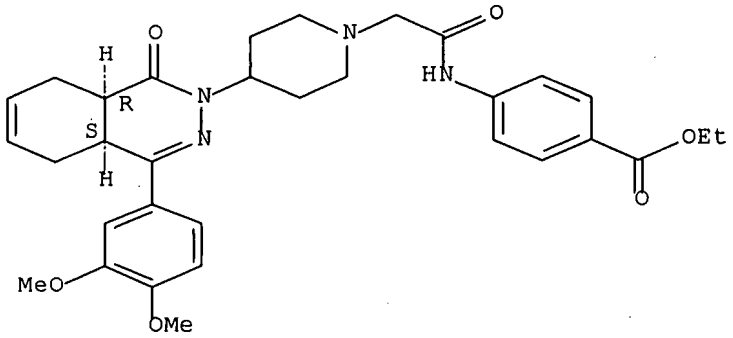
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



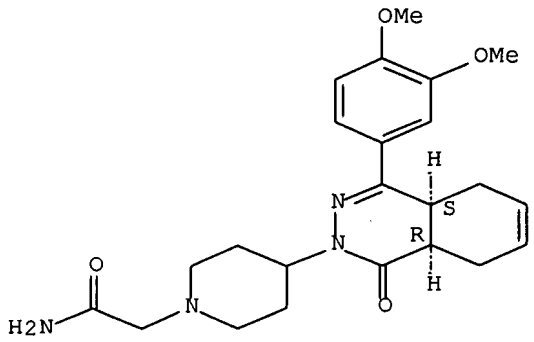
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

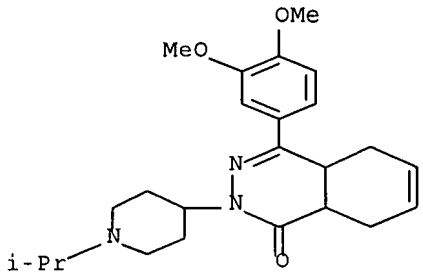


RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.

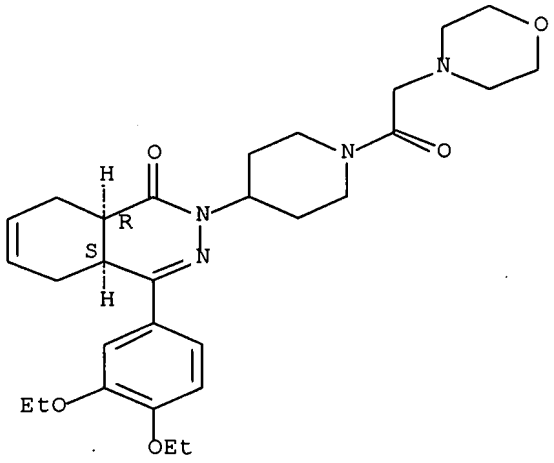


RN 596102-01-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methylethyl)-4-piperidinyl]- (CA INDEX NAME)



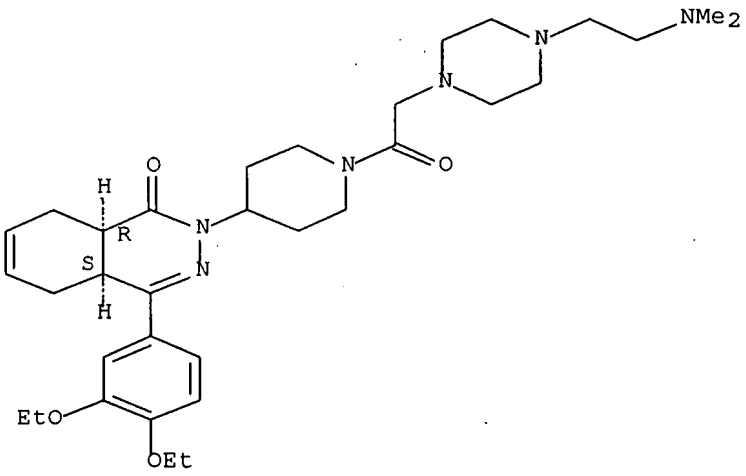
RN 596102-07-7 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-morpholinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 596102-09-9 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[4-[2-(dimethylamino)ethyl]-1-piperazinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM A61K031-4425
ICS A61K031-4523; A61K031-4375; A61K045-06; A61P011-06; A61P011-08
CC 1-9 (**Pharmacology**)
Section cross-reference(s): **63**
IT 72-69-5, Nortriptyline 91-81-6, Tripelenamine 3964-81-6, Azatadine 15686-51-8 25523-97-1 50679-08-8, Terfenadine 58581-89-8, Azelastine 58761-87-8 64294-95-7, Setastine 69372-19-6, Pemirolast 75970-99-9, Norastemizole 79516-68-0 79794-75-5, Loratadine 80012-43-7, Epinastine 83799-24-0, Fexofenadine 83881-51-0, Cetirizine 83881-51-0D, Cetirizine, derivs. 87233-61-2, Emedastine 87848-99-5, Acrivastine 90729-43-4, Ebastine 100643-71-8, Desloratadine 108612-45-9, Mizolastine 125602-71-3 130018-77-8 130018-77-8D, Levocetirizine, derivs. 132210-43-6, Cipamfylline 135637-46-6, Atizoram 136145-07-8, Arofylline 139226-28-1, Darbufelone 145261-31-0, ORG 20241 150756-35-7, Efletirizine 153259-65-5, Cilomilast 158876-82-5, Rupatadine 161522-25-4, HSR 609 162278-09-3, V 11294A 162401-32-3, Roflumilast 175013-92-0 189940-24-7, SH 636 192819-27-5, CDC 801 207993-12-2, Pumafentrine 245329-99-1, CI 1018 257892-33-4, AWD 12-281 329306-27-6, Lirimilast 337359-69-0 337359-70-3 337359-71-4 337359-72-5 337359-73-6 337359-74-7 337359-75-8 337359-76-9 337532-27-1 337532-29-3 444658-74-6, CDC 998 444659-40-9, IC 485 444659-42-1, KW 4490 444659-43-2, Sch 351591 444659-44-3, AWD 12-343 **449760-14-9 449760-15-0 449760-16-1 449760-17-2 449760-19-4 449760-20-7 449760-22-9 449760-23-0 449760-24-1 449760-25-2 449760-26-3 449760-28-5 449760-29-6 449760-30-9 449760-35-4 449760-40-1 449760-42-3 449760-47-8 449760-48-9 449760-49-0 449760-50-3 449760-51-4 449760-52-5 449760-53-6 449760-56-9 449760-57-0 449760-58-1** 467421-06-3, CC 1088 **596102-01-1 596102-07-7 596102-09-9**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 (PDE4) inhibitor or PDE3/4 inhibitor combination with histamine receptor antagonist for treatment of respiratory disease)
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:832801 HCAPLUS Full-text
DOCUMENT NUMBER: 137:337906
TITLE: Preparation of phthalazinones as phosphodiesterase 4/7 inhibitors.
INVENTOR(S): Hatzelmann, Armin; Marx, Degenhard; Steinhilber, Wolfram; Sterk, Geert Jan
PATENT ASSIGNEE(S): Altana Pharma A.-G., Germany
SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085906	A2	20021031	WO 2002-EP4438	20020423 <--
WO 2002085906	A3	20021219		
W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2445233	A1	20021031	CA 2002-2445233	20020423 <--
AU 2002317733	A1	20021105	AU 2002-317733	20020423 <--
EP 1385848	A2	20040204	EP 2002-747291	20020423 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
EE 200300514	A	20040216	EE 2003-514	20020423 <--
HU 2003003998	A2	20040528	HU 2003-3998	20020423 <--
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CN 1503792	A	20040609	CN 2002-808742	20020423 <--
BR 2002009149	A	20040713	BR 2002-9149	20020423 <--
JP 2004526789	T	20040902	JP 2002-583433	20020423 <--
NZ 529221	A	20050429	NZ 2002-529221	20020423 <--
MX 2003PA09583	A	20040212	MX 2003-PA9583	20031020 <--
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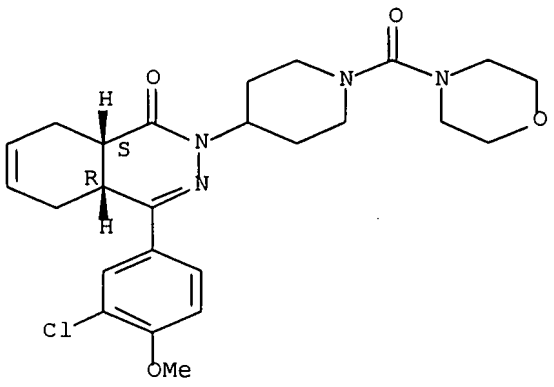
US 7186710	B2	20070306		
NO 2003004773	A	20031210	NO 2003-4773	20031024 <--
BG 108294	A	20040930	BG 2003-108294	20031027 <--
ZA 2003008930	A	20040609	ZA 2003-8930	20031117 <--
IN 2003MN01079	A	20050429	IN 2003-MN1079	20031124 <--
PRIORITY APPLN. INFO.:			EP 2001-110228 A	20010425 <--
			WO 2002-EP4438 W	20020423 <--

OTHER SOURCE(S): MARPAT 137:337906
ED Entered STN: 01 Nov 2002
AB Title compds. (I; R1 = alkoxy, fluoroalkoxy; R2 = F, Br, Cl; R3, R4 = H; R3R4 = bond; R5 = alkyl, cycloalkyl, cycloalkylmethyl, alkenyl, alkynyl, phenylalkenyl, polycycloalkyl, naphthyl, pyridyl, pyrazinyl, pyridazinyl, pyrimidinyl, etc.), were prepared Thus, cis-4-(3-chloro-4-methoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (preparation given) was stirred 16 h with morpholine-4-carbonyl chloride in pyridine to give cis-4-(3-chloro-4-methoxyphenyl)-2-[1-(1-morpholin-4-ylmethanoyl)piperidin- 4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one. The latter inhibited PDE4 and PDE7 with -log IC50 = 8.64 and 7.64, resp.
IT **474122-96-8P 474122-97-9P 474122-98-0P**
474122-99-1P 474123-17-6P 474123-26-7P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phthalazinones as phosphodiesterase 4/7 inhibitors)

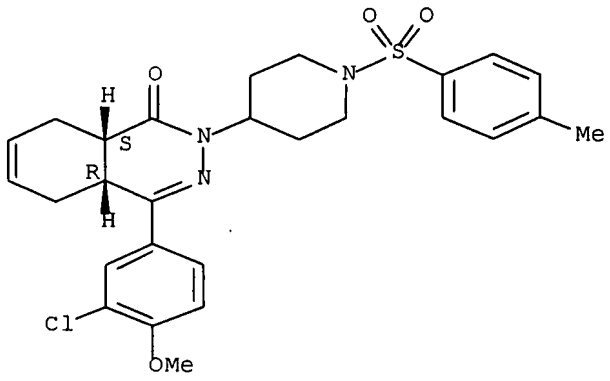
RN 474122-96-8 HCAPLUS
CN Morpholine, 4-[[4-[(4aR,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



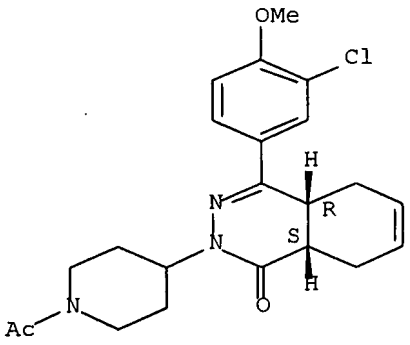
RN 474122-97-9 HCAPLUS
CN Piperidine, 4-[(4aR,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



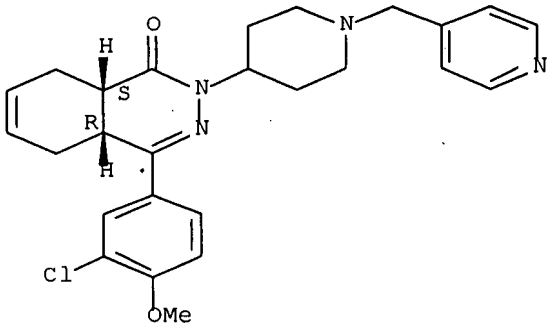
RN 474122-98-0 HCAPLUS
CN Piperidine, 1-acetyl-4-[(4aR,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



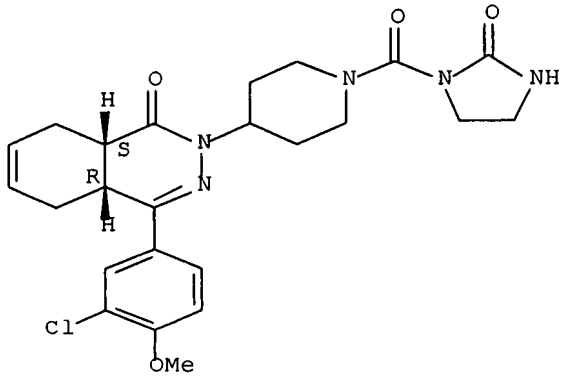
RN 474122-99-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aR,8aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



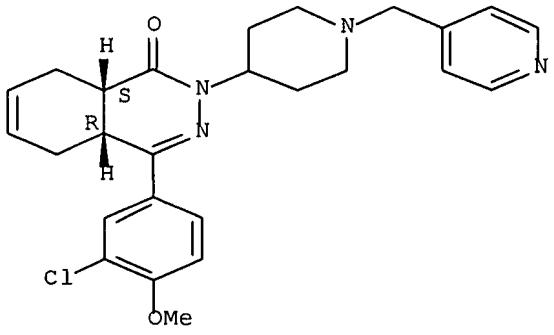
RN 474123-17-6 HCAPLUS
CN Piperidine, 4-[(4aR,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(2-oxo-1-imidazolidinyl)carbonyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 474123-26-7 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, hydrochloride, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

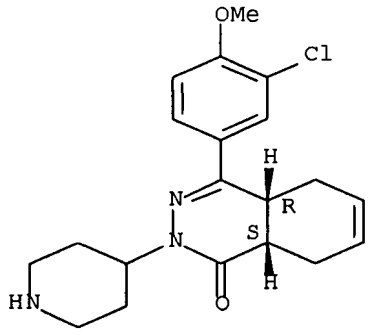
Relative stereochemistry.



●x HCl

IT **474123-18-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phthalazinones as phosphodiesterase 4/7 inhibitors)
RN 474123-18-7 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, (4aR,8aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



IC ICM C07D487-00
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
IT **474122-96-8P 474122-97-9P 474122-98-0P**
474122-99-1P 474123-00-7P 474123-01-8P 474123-02-9P
474123-03-0P 474123-04-1P 474123-05-2P 474123-06-3P 474123-07-4P

474123-08-5P 474123-09-6P 474123-10-9P 474123-11-0P 474123-12-1P
474123-13-2P 474123-14-3P 474123-15-4P 474123-16-5P
474123-17-6P 474123-26-7P 474123-27-8P 474123-28-9P
474123-29-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phthalazinones as phosphodiesterase 4/7 inhibitors)

IT 244077-36-9P 244077-38-1P 380226-98-2P 380226-99-3P 380227-00-9P
474123-18-7P 474123-19-8P 474123-20-1P 474123-21-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phthalazinones as phosphodiesterase 4/7 inhibitors)

L18 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:637671 HCAPLUS Full-text
DOCUMENT NUMBER: 137:185496
TITLE: Preparation of piperidinyl benzopyridazine derivatives as PDE4 inhibitors for treatment of airway disorders
INVENTOR(S): Hatzelmann, Armin; Bundschuh, Daniela; Kley, Hans-peter; Timmerman, Hendrik; Christiaans, Johannes A. M.; Grundler, Gerhard; Gutterer, Beate; Sterk, Geert Jan
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik Gmbh, Germany
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064584	A1	20020822	WO 2002-EP1547	20020214 <--
W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2438520	A1	20020822	CA 2002-2438520	20020214 <--
AU 2002234634	A1	20020828	AU 2002-234634	20020214 <--
AU 2002234634	B2	20070726		
EE 200300311	A	20031015	EE 2003-311	20020214 <--
EP 1362044	A1	20031119	EP 2002-701277	20020214 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003003193	A2	20031229	HU 2003-3193	20020214 <--
HU 200303193	A3	20070828		
BR 2002007278	A	20040210	BR 2002-7278	20020214 <--
JP 2004518727	T	20040624	JP 2002-564515	20020214 <--
CN 1524080	A	20040825	CN 2002-805038	20020214 <--
NZ 527424	A	20050225	NZ 2002-527424	20020214 <--
IN 2003MN00668	A	20050211	IN 2003-MN668	20030701 <--
US 2004067946	A1	20040408	US 2003-467832	20030813 <--
US 6953853	B2	20051011		
NO 2003003618	A	20031015	NO 2003-3618	20030814 <--
MX 2003PA07310	A	20031204	MX 2003-PA7310	20030815 <--
BG 108124	A	20040831	BG 2003-108124	20030821 <--
ZA 2003006815	A	20040617	ZA 2003-6815	20030901 <--

US 2005234062	A1	20051020	US 2005-143721		20050603 <--
US 7179810	B2	20070220			
US 2007129373	A1	20070607	US 2006-647191		20061229 <--
PRIORITY APPLN. INFO.:			EP 2001-103496	A	20010215 <--
			WO 2002-EP1547	W	20020214 <--
			US 2003-467832	A1	20030813 <--
			US 2005-143721	A1	20050603

OTHER SOURCE(S): MARPAT 137:185496

ED Entered STN: 23 Aug 2002

AB Piperidinyl benzopyridazine derivs. [I; wherein R1 and R2 = H, or together form an addnl. bond; R3 = substituted benzene, benzopyran derivative; R4 = (C1-C4)alkoxy, optionally substituted with fluorine] were prepared Thus, to a solution of (4aS,8aR)-4-(3,4-diethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (synthetic preparation given) and p-TsCl in pyridine is stirred to give (4aS,8aR)-4-(3,4-diethoxyphenyl)-2- [1-(toluene-4-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin- 1-one. The prepared compds. are effective PDE4 inhibitors useful in the treatment of airway disorders.

IT **449760-14-9P 449760-15-0P 449760-16-1P**
449760-17-2P 449760-18-3P 449760-19-4P
449760-20-7P 449760-21-8P 449760-22-9P
449760-23-0P 449760-24-1P 449760-25-2P
449760-26-3P 449760-27-4P 449760-28-5P
449760-29-6P 449760-30-9P 449760-31-0P
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449760-38-7P 449760-39-8P 449760-40-1P
449760-41-2P 449760-42-3P 449760-43-4P
449760-44-5P 449760-47-8P 449760-48-9P
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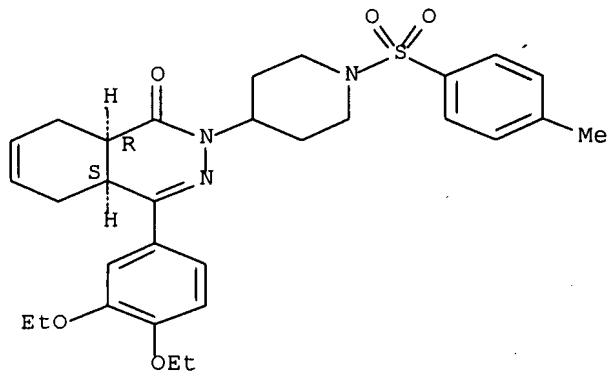
449760-52-5P 449760-53-6P 449760-54-7P
449760-55-8P 449760-56-9P 449760-57-0P
449760-58-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinyl benzopyridazine derivs. as PDE4 inhibitors for treatment of airway disorders)

RN 449760-14-9 HCAPLUS

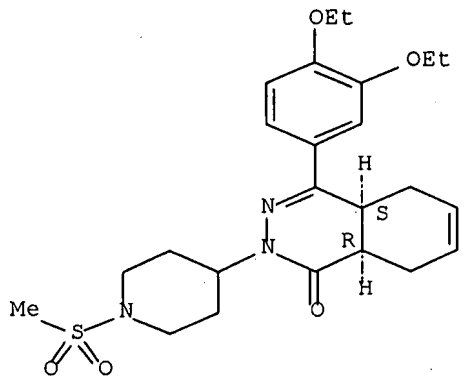
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



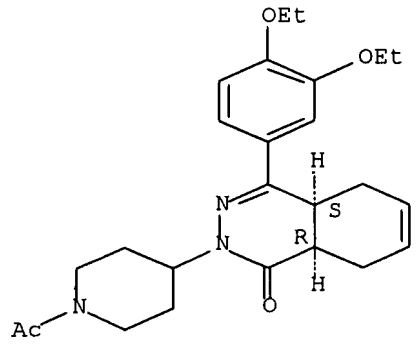
RN 449760-15-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



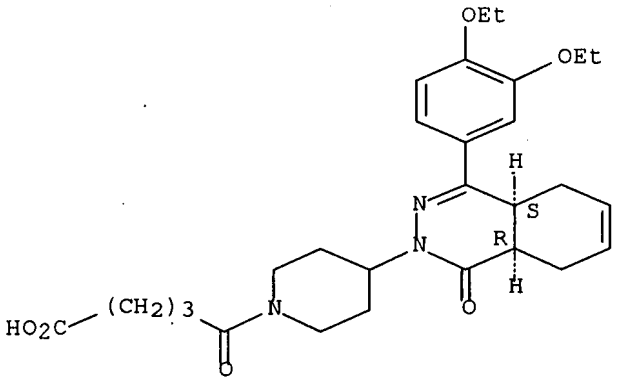
RN 449760-16-1 HCAPLUS
CN Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



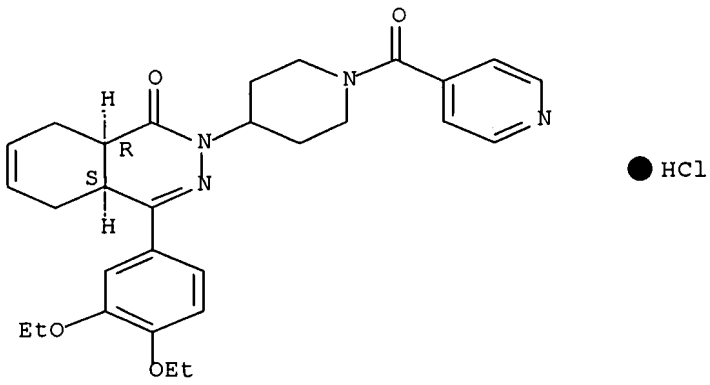
RN 449760-17-2 HCAPLUS
CN 1-Piperidinepentanoic acid, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-δ-oxo- (CA INDEX NAME)

Absolute stereochemistry.



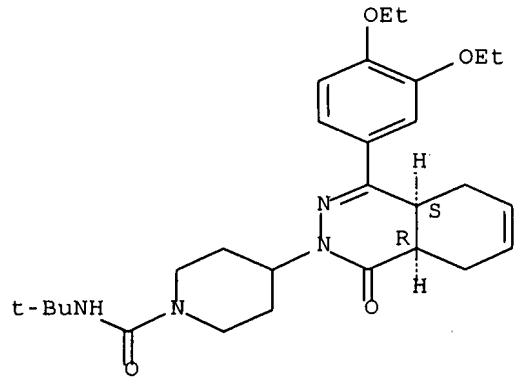
RN 449760-18-3 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



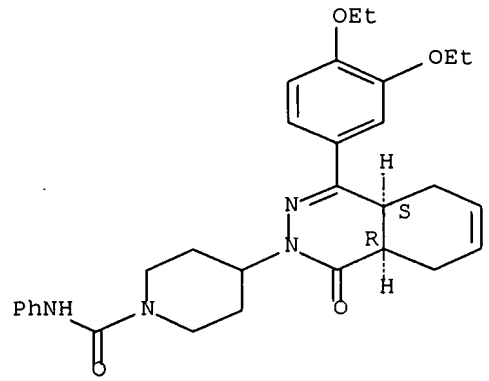
RN 449760-19-4 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



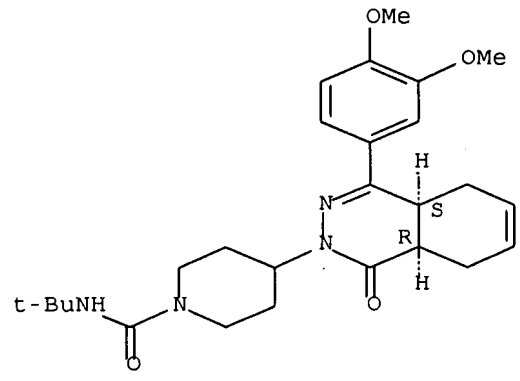
RN 449760-20-7 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (CA INDEX NAME)

Absolute stereochemistry.



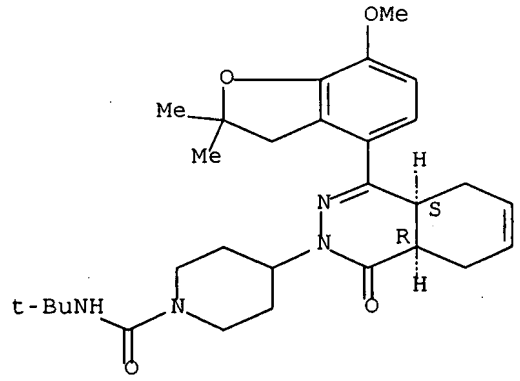
RN 449760-21-8 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-22-9 HCAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (CA INDEX NAME)

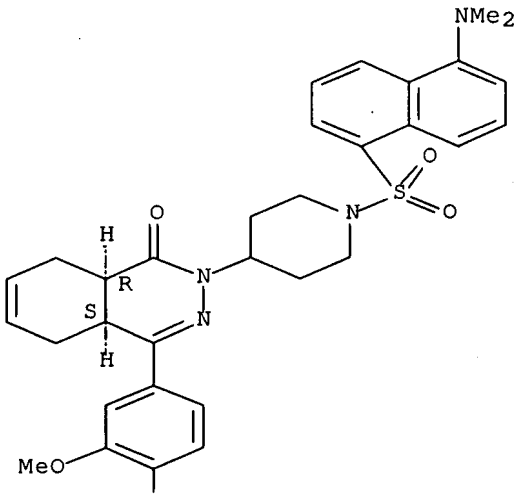
Relative stereochemistry.



RN 449760-23-0 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

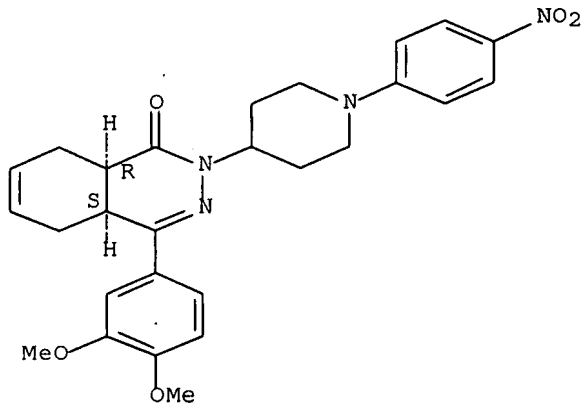
PAGE 1-A



OMe

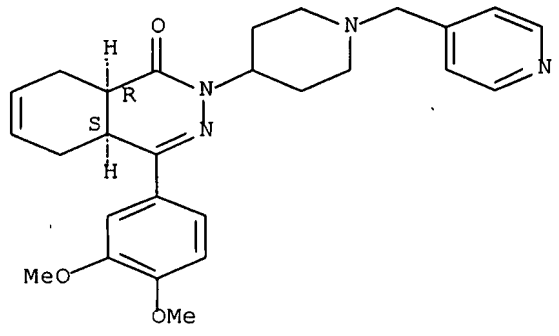
RN 449760-24-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



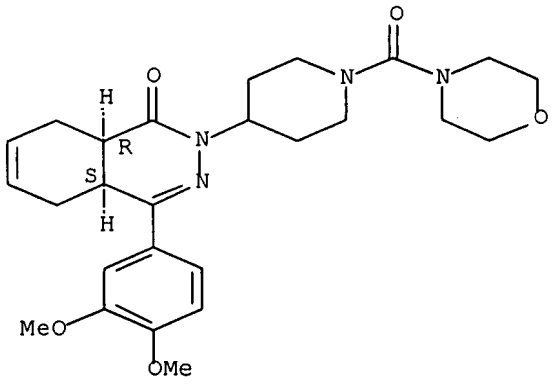
RN 449760-25-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



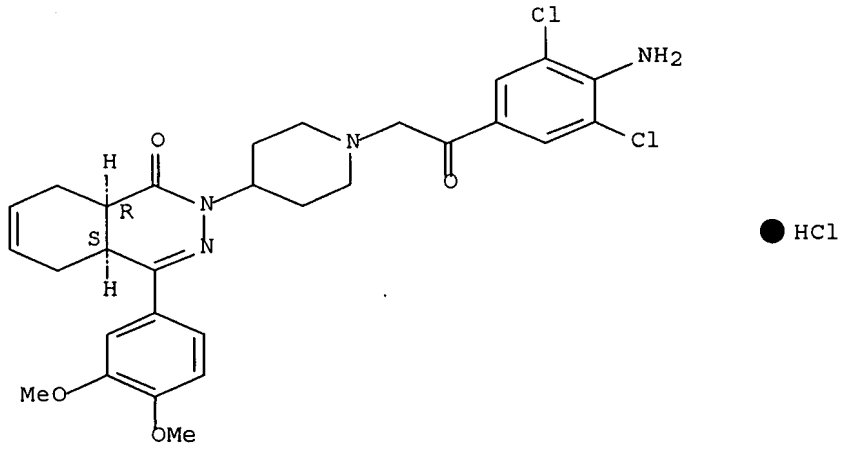
RN 449760-26-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



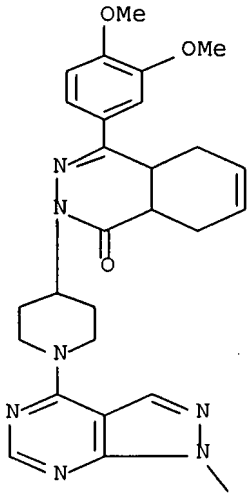
RN 449760-27-4 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-28-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (CA INDEX NAME)

PAGE 1-A



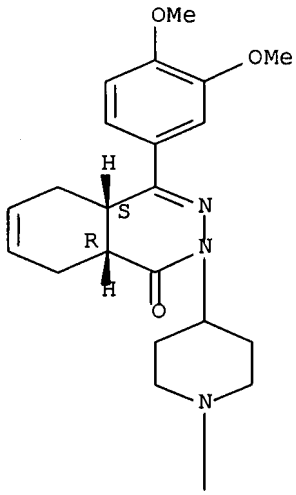
PAGE 2-A

Me

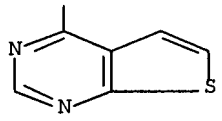
RN 449760-29-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

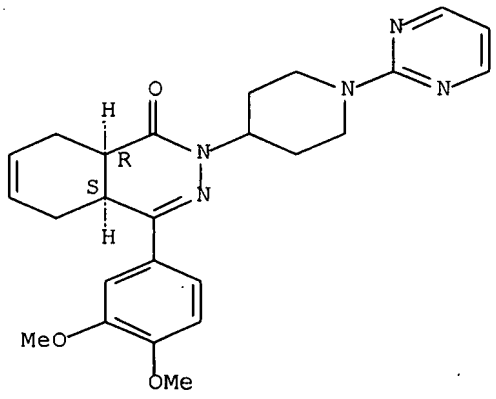


PAGE 2-A



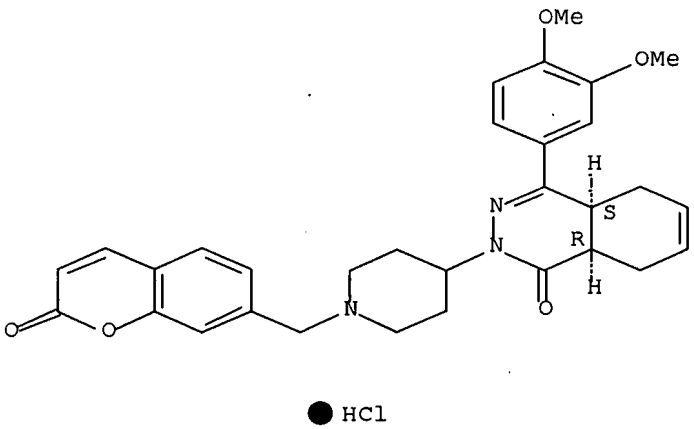
RN 449760-30-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



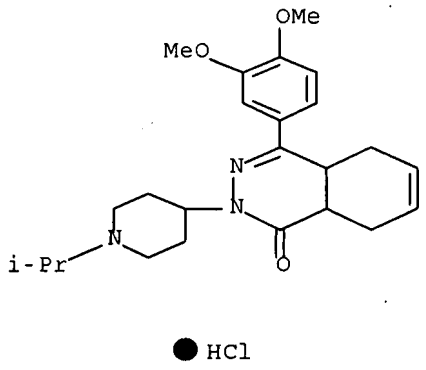
RN 449760-31-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



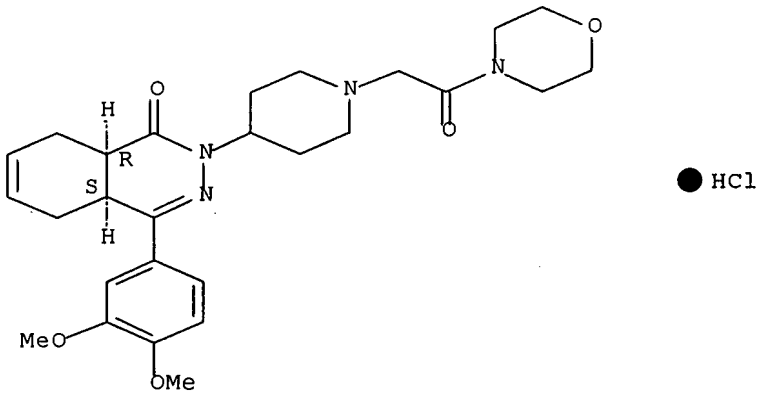
● HCl

RN 449760-32-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methylethyl)-4-piperidinyl]-, monohydrochloride (9CI) (CA INDEX NAME)



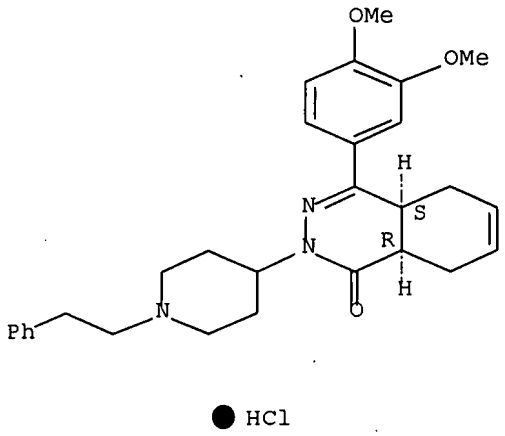
RN 449760-33-2 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



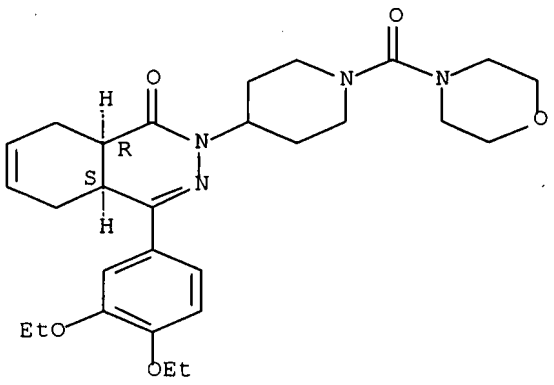
RN 449760-34-3 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



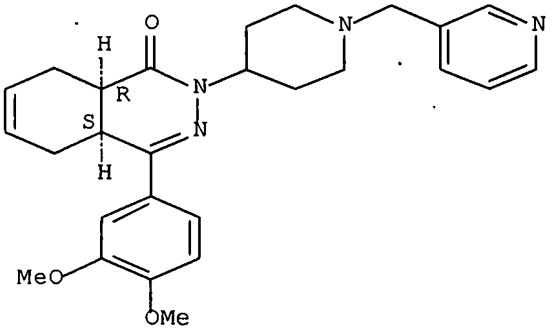
RN 449760-35-4 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-36-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, dihydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

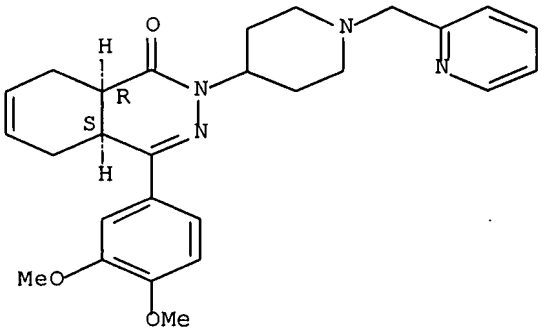
Absolute stereochemistry.



●2 HCl

RN 449760-37-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, dihydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

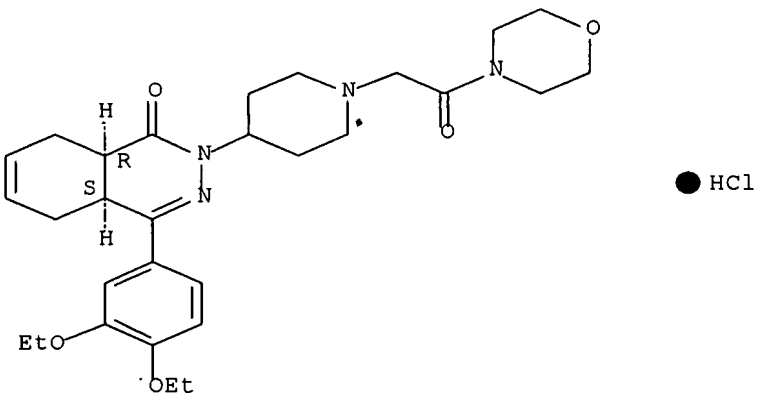
Absolute stereochemistry.



●2 HCl

RN 449760-38-7 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

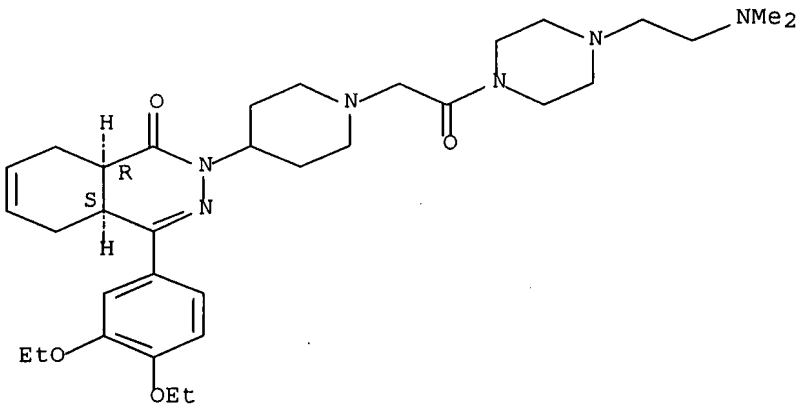
Absolute stereochemistry.



RN 449760-39-8 HCAPLUS
CN 1-Piperazineethanamine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl-, trihydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

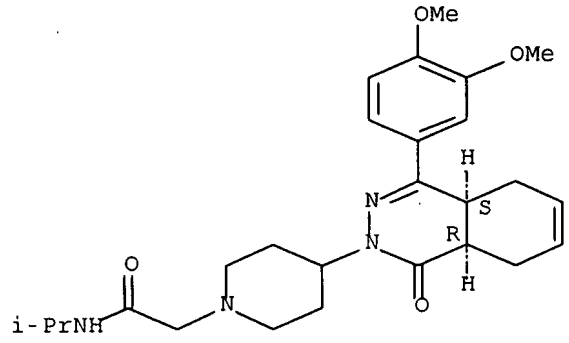


PAGE 2-A

3 HCl

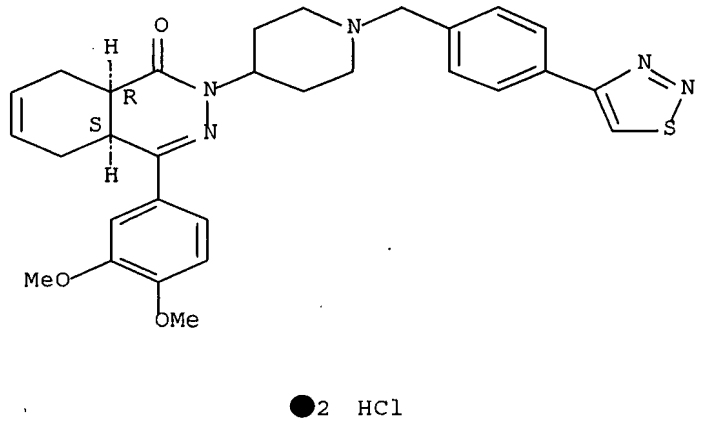
RN 449760-40-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (CA INDEX NAME)

Absolute stereochemistry.



RN 449760-41-2 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, dihydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

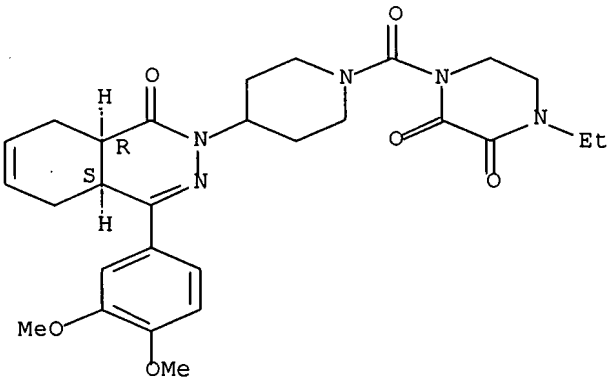
Absolute stereochemistry.



●2 HCl

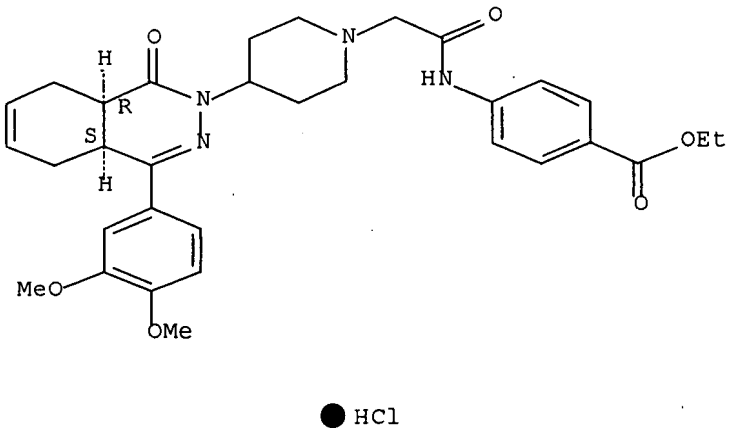
RN 449760-42-3 HCAPLUS
CN 2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl- (CA INDEX NAME)

Absolute stereochemistry.



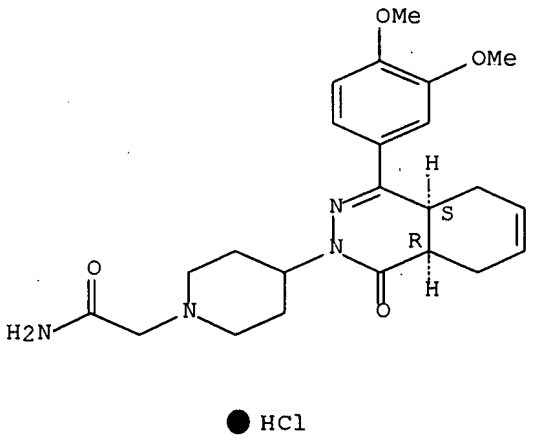
RN 449760-43-4 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



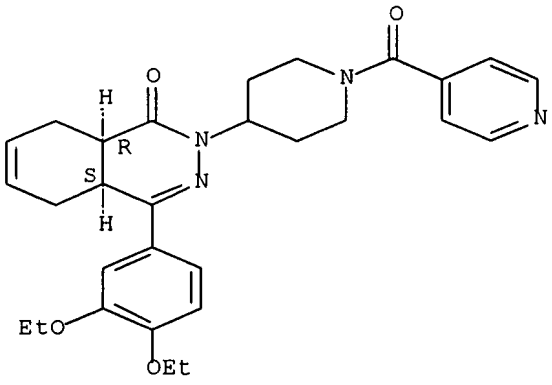
RN 449760-44-5 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



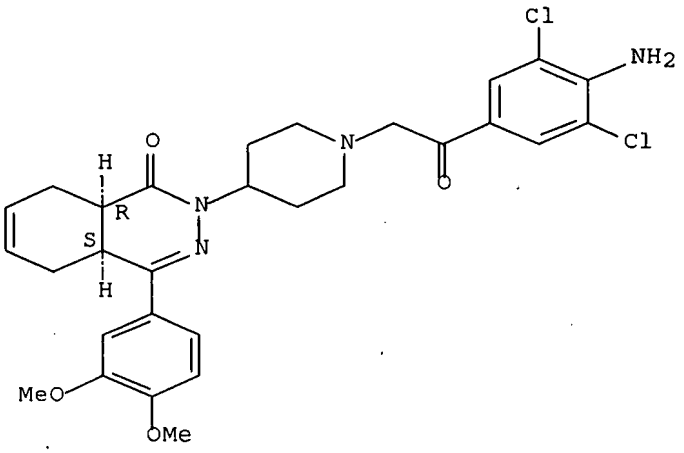
RN 449760-47-8 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



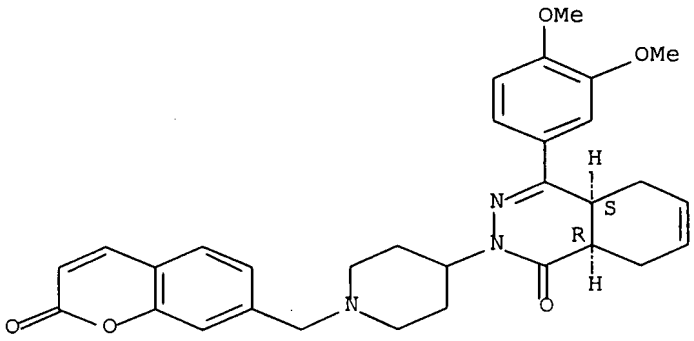
RN 449760-48-9 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



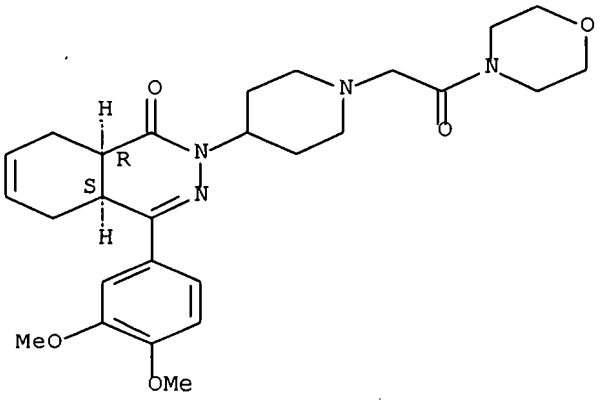
RN 449760-49-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



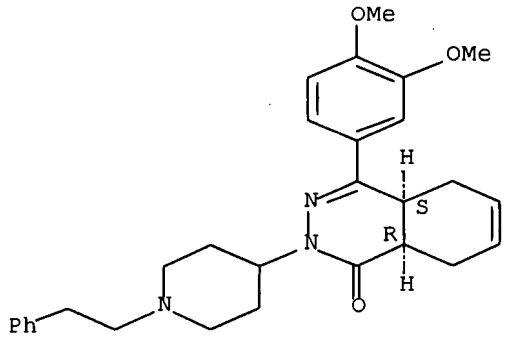
RN 449760-50-3 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



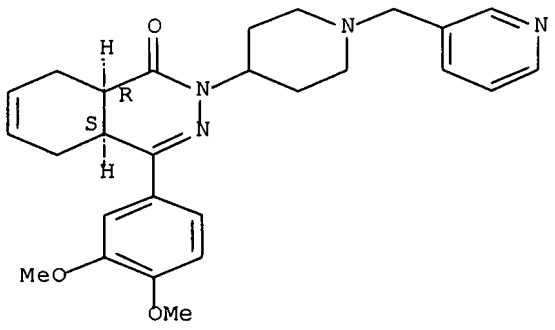
RN 449760-51-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



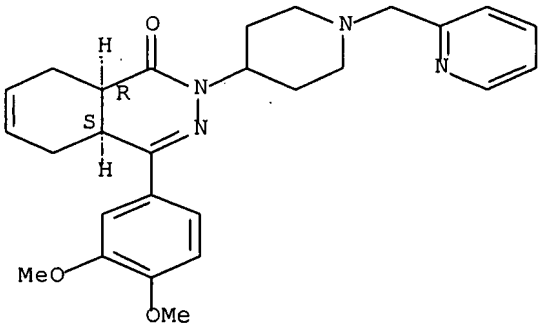
RN 449760-52-5 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



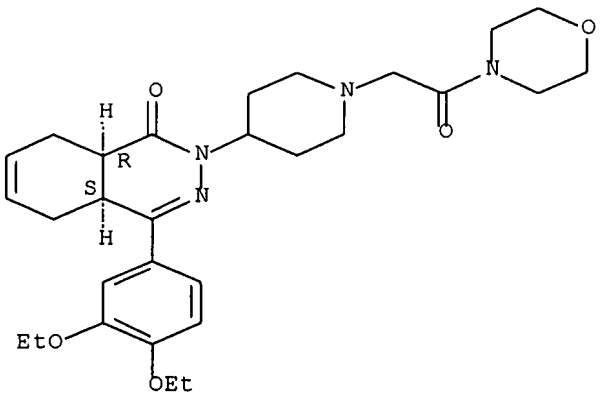
RN 449760-53-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



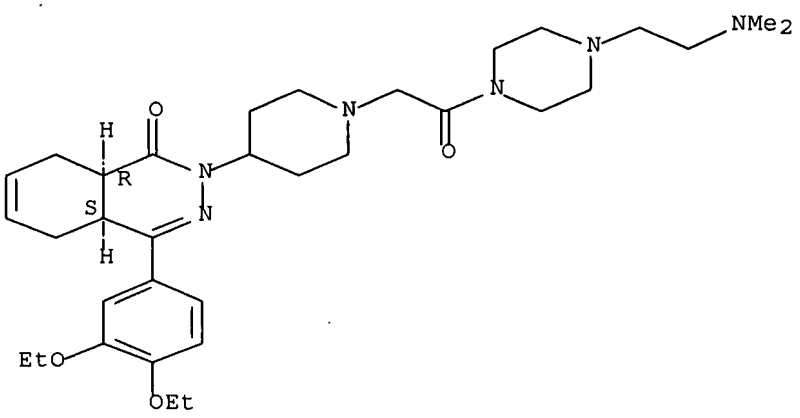
RN 449760-54-7 HCAPLUS
CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



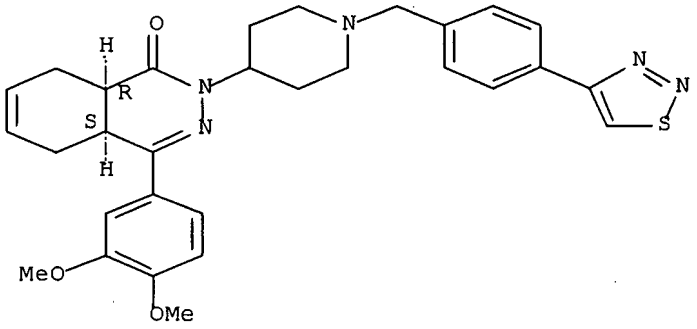
RN 449760-55-8 HCAPLUS
CN 1-Piperazineethanamine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



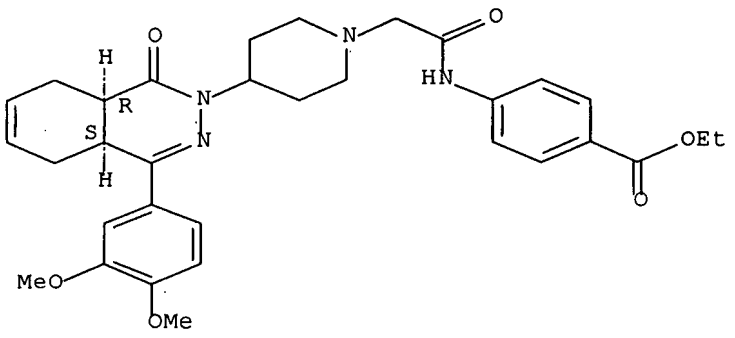
RN 449760-56-9 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



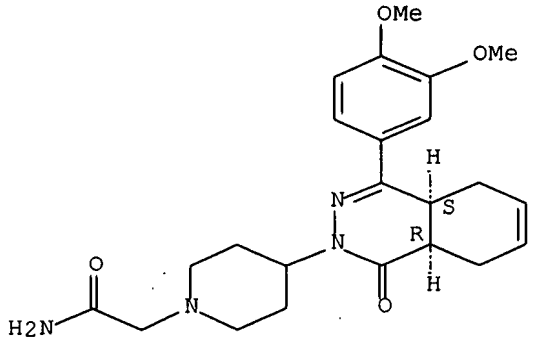
RN 449760-57-0 HCAPLUS
CN Benzoic acid, 4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



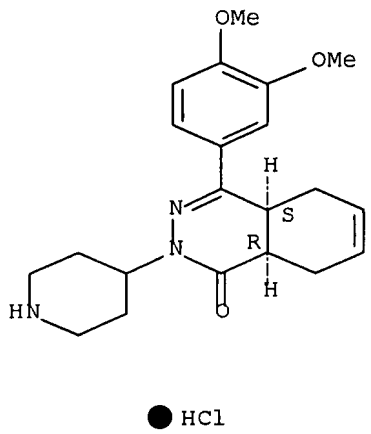
RN 449760-58-1 HCAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (CA INDEX NAME)

Absolute stereochemistry.



IT **380226-97-1P 380227-12-3P 380227-13-4P**
449760-45-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinyl benzopyridazine derivs. as PDE4 inhibitors for treatment of airway disorders)
RN 380226-97-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

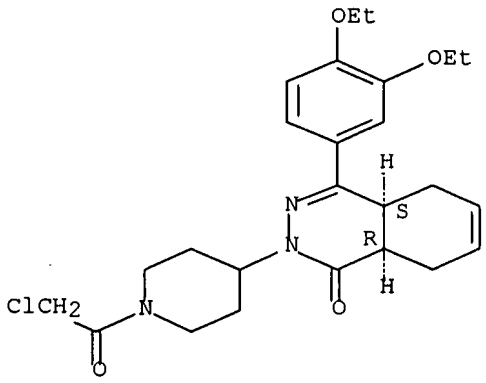
Absolute stereochemistry.



● HCl

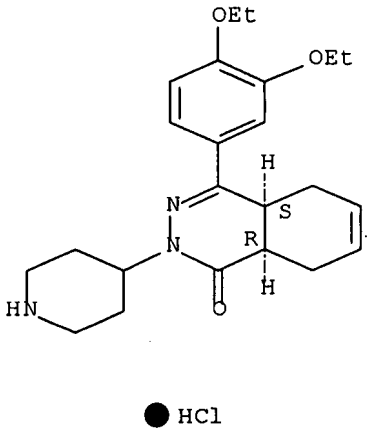
RN 380227-12-3 HCAPLUS
CN Piperidine, 1-(chloroacetyl)-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380227-13-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

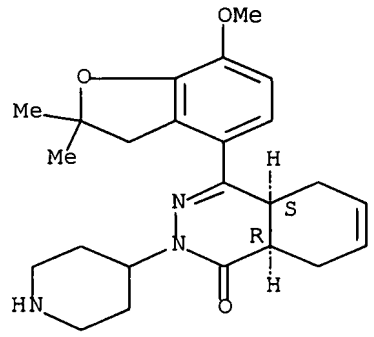
Absolute stereochemistry.



● HCl

RN 449760-45-6 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, (4aR,8aS)-rel- (CA INDEX NAME)

Relative stereochemistry.



IC ICM C07D401-04
ICS C07D237-32; A61K031-50; C07D407-04; A61K031-4427; A61P029-00
CC 28-15 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 63
IT **449760-14-9P 449760-15-0P 449760-16-1P**
449760-17-2P 449760-18-3P 449760-19-4P
449760-20-7P 449760-21-8P 449760-22-9P
449760-23-0P 449760-24-1P 449760-25-2P
449760-26-3P 449760-27-4P 449760-28-5P
449760-29-6P 449760-30-9P 449760-31-0P
449760-32-1P 449760-33-2P 449760-34-3P
449760-35-4P 449760-36-5P 449760-37-6P
449760-38-7P 449760-39-8P 449760-40-1P
449760-41-2P 449760-42-3P 449760-43-4P
449760-44-5P 449760-47-8P 449760-48-9P
449760-49-0P 449760-50-3P 449760-51-4P
449760-52-5P 449760-53-6P 449760-54-7P
449760-55-8P 449760-56-9P 449760-57-0P
449760-58-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of piperidinyl benzopyridazine derivs. as PDE4 inhibitors for treatment of airway disorders)
IT **380226-97-1P** 380226-98-2P 380226-99-3P 380227-00-9P
380227-12-3P 380227-13-4P 449760-45-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinyl benzopyridazine derivs. as PDE4 inhibitors for treatment of airway disorders)
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:904118 HCAPLUS Full-text
DOCUMENT NUMBER: 136:37625
TITLE: Preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Bundschuh, Daniela; Eltze, Manfrid; Van der Laan, Yvonne; Timmermann, Hendrik; Christiaans, Johannes; Brundel, Paulus; Sterk, Geert
PATENT ASSIGNEE(S): Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany; Byk Nederland B.V.
SOURCE: PCT Int. Appl., 79 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001094319	A1	20011213	WO 2001-EP6230	20010601 <--
W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
CA 2411351	A1	20011213	CA 2001-2411351	20010601 <--
EP 1296956	A1	20030402	EP 2001-936419	20010601 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011440	A	20030603	BR 2001-11440	20010601 <--
JP 2003535850	T	20031202	JP 2002-501869	20010601 <--
HU 2003001240	A2	20031229	HU 2003-1240	20010601 <--
NZ 522882	A	20040730	NZ 2001-522882	20010601 <--
IN 2002MN01591	A	20050318	IN 2002-MN1591	20021111 <--
ZA 2002009598	A	20030729	ZA 2002-9598	20021126 <--
NO 2002005811	A	20030204	NO 2002-5811	20021203 <--
MX 2002PA12042	A	20040819	MX 2002-PA12042	20021205 <--
US 2003195215	A1	20031016	US 2003-296411	20030402 <--
US 6933296	B2	20050823		

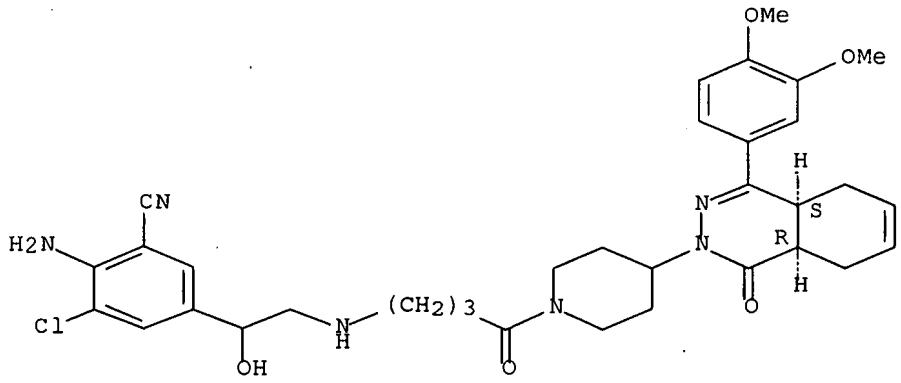
PRIORITY APPLN. INFO.: EP 2000-111795 A 20000605 <--
WO 2001-EP6230 W 20010601 <--

OTHER SOURCE(S): MARPAT 136:37625
ED Entered STN: 14 Dec 2001
AB The title compds. [I; Ar1 = substituted Ph, dihydrobenzofuranyl; R6, R7 = H, alkyl; or R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form II-V; A = CmH2mYXCnH2n, YXCmH2mZCnH2n; X = a bond, O, S, etc.; Y = a bond, phenylene, cycloalkylene, etc.; Z = O, S, SO2, etc.; m = 0-4; n = 1-4; R8 = H, alkyl; Ar2 = 8-hydroxy-1H-quinolin-2-on-5-yl, substituted Ph], useful as novel effective bronchial therapeutics, were prepared The general procedures for preparation of compds. I such as (cis)-VI.fumarate were described. Biol. data for compds. I were given.
IT **380226-56-2P 380226-64-2P 380226-65-3P**
380226-67-5P 380226-69-7P 380226-71-1P
380226-72-2P 380226-74-4P 380226-77-7P
380226-78-8P 380226-80-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors)
RN 380226-56-2 HCAPLUS
CN Piperidine, 1-[4-[[2-(4-amino-3-chloro-5-cyanophenyl)-2-hydroxyethyl]amino]-1-oxobutyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-55-1
CMF C34 H41 Cl N6 O5

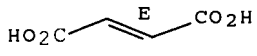
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

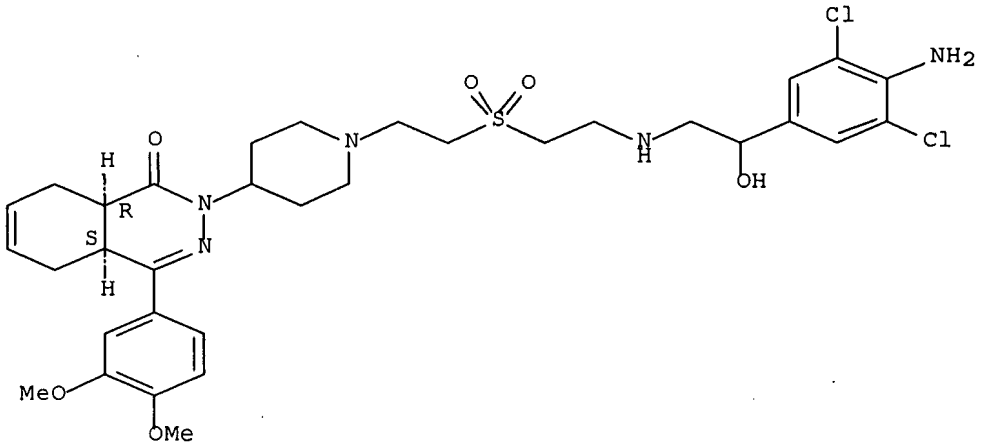


RN 380226-64-2 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-[2-[[2-[[2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]ethyl]sulfonyl]ethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-63-1
CMF C33 H43 Cl2 N5 O6 S

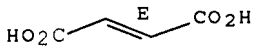
Absolute stereochemistry.



CM 2

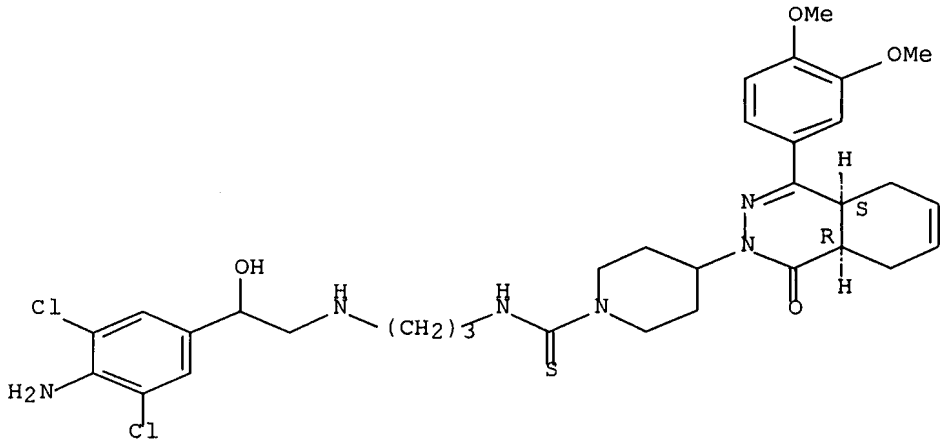
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 380226-65-3 HCAPLUS
CN 1-Piperidinecarbothioamide, N-[3-[[2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]propyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



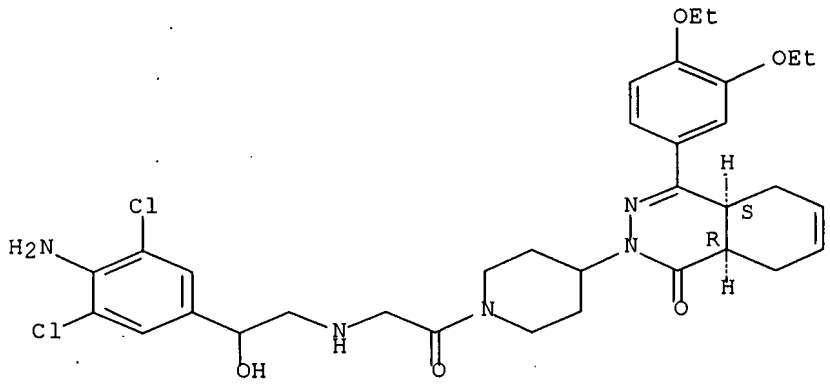
RN 380226-67-5 HCAPLUS

CN Piperidine, 1-[[[2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]acetyl]-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-66-4
CMF C33 H41 Cl2 N5 O5

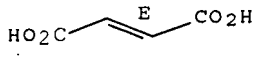
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

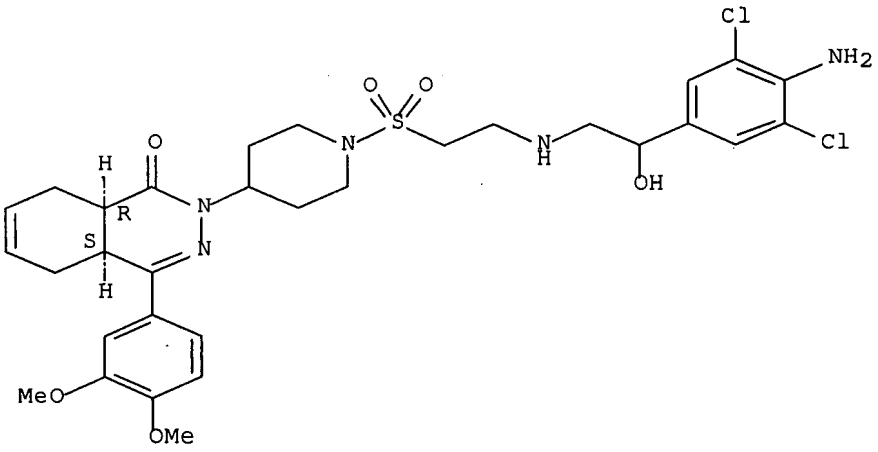


RN 380226-69-7 HCAPLUS
CN Piperidine, 1-[[2-[[2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]ethyl]sulfonyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-68-6
CMF C31 H39 Cl2 N5 O6 S

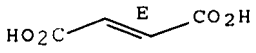
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

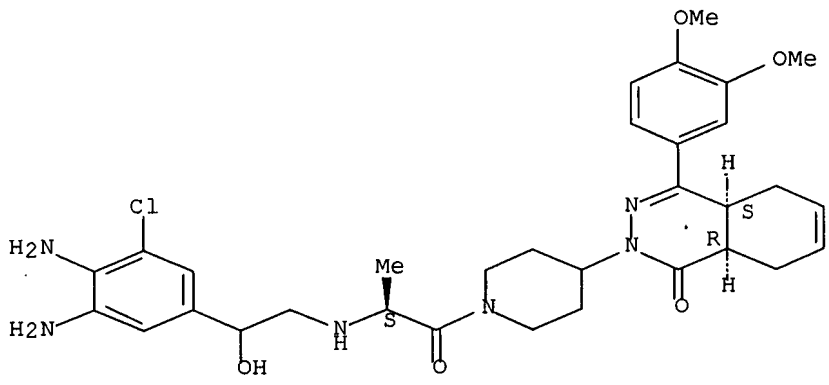


RN 380226-71-1 HCAPLUS
CN Piperidine, 1-[(2S)-2-[[2-(3,4-diamino-5-chlorophenyl)-2-hydroxyethyl]amino]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-70-0
CMF C32 H41 Cl N6 O5

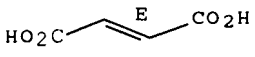
Absolute stereochemistry.



CM 2

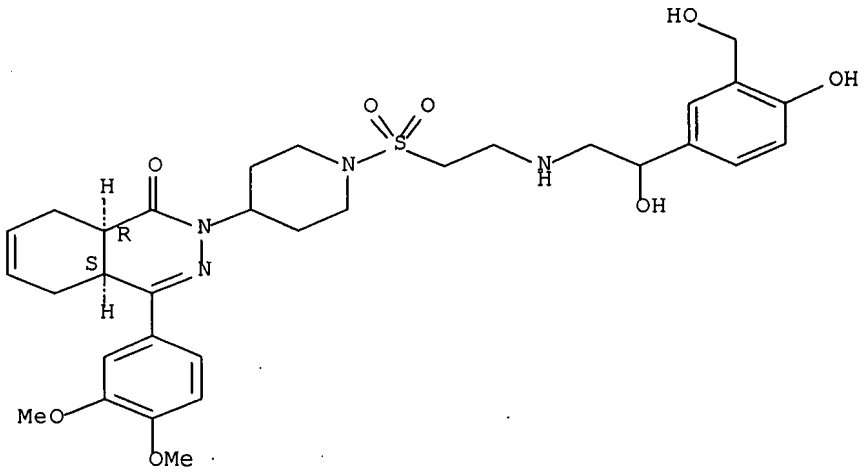
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 380226-72-2 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[2-[[2-hydroxy-2-[4-hydroxy-3-(hydroxymethyl)phenyl]ethyl]amino]ethyl]sulfonyl]- (9CI) (CA INDEX NAME)

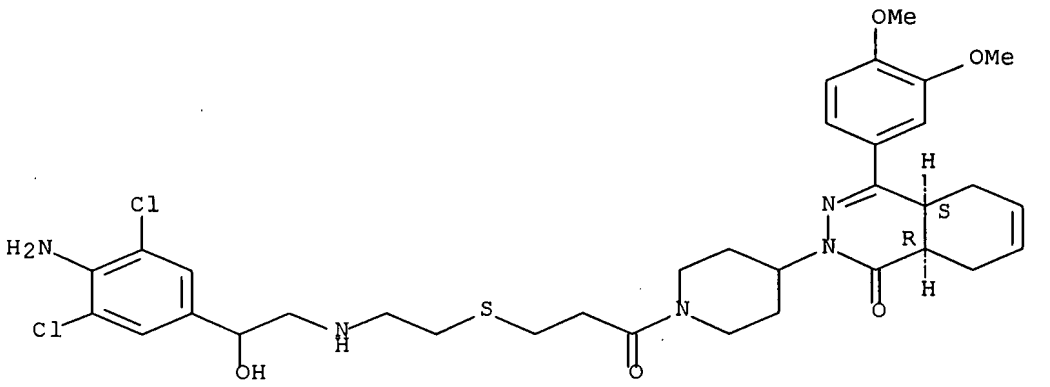
Absolute stereochemistry.



RN 380226-74-4 HCAPLUS
CN Piperidine, 1-[3-[[2-[[2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]ethyl]thio]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

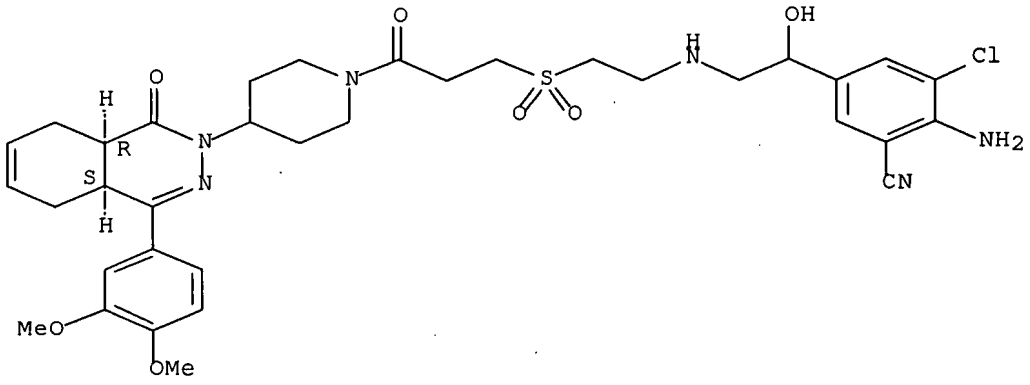


PAGE 2-A

● HCl

RN 380226-77-7 HCAPLUS
CN Piperidine, 1-[3-[[2-[[2-(4-amino-3-chloro-5-cyanophenyl)-2-hydroxyethyl]amino]ethyl]sulfonyl]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

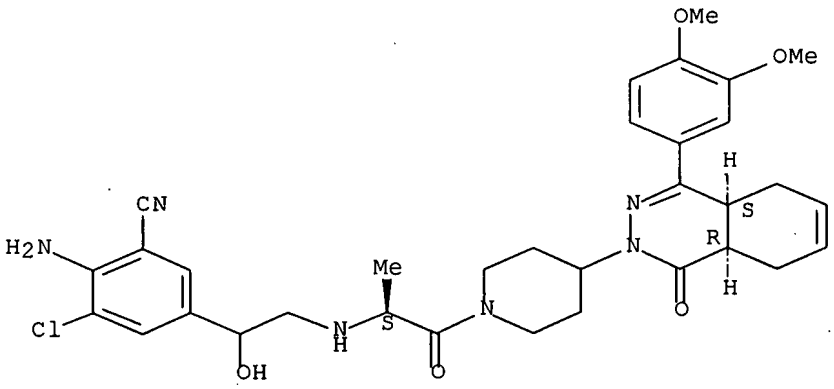
Absolute stereochemistry.



RN 380226-78-8 HCAPLUS
CN Piperidine, 1-[(2S)-2-[[2-(4-amino-3-chloro-5-cyanophenyl)-2-hydroxyethyl]amino]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 2-A

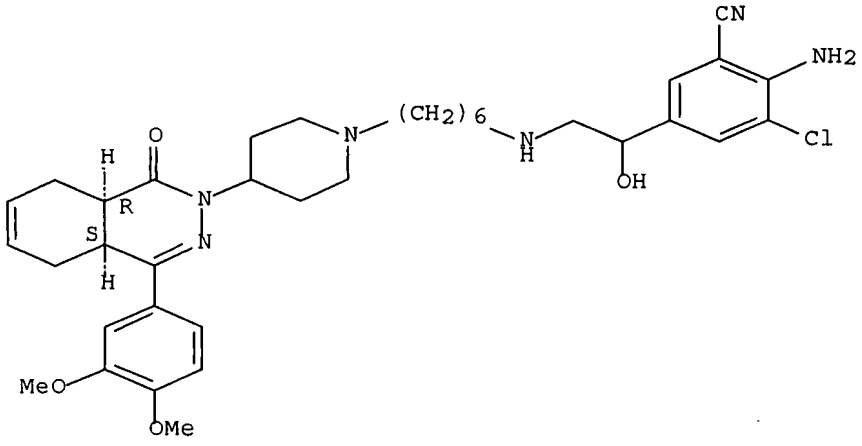
● HCl

RN 380226-80-2 HCAPLUS
CN Benzonitrile, 2-amino-3-chloro-5-[2-[[6-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]hexyl]amino]-1-hydroxyethyl]-, (2E)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-79-9
CMF C36 H47 Cl N6 O4

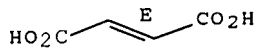
Absolute stereochemistry.



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



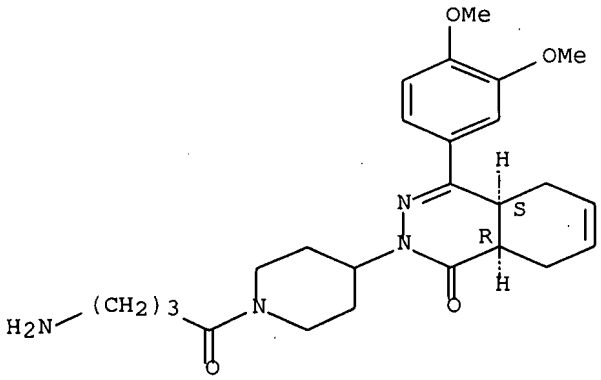
IT **380226-94-8P 380226-95-9P 380226-96-0P**
380226-97-1P 380227-08-7P 380227-10-1P
380227-11-2P 380227-12-3P 380227-13-4P
380227-14-5P 380227-15-6P 380227-16-7P
380227-17-8P 380227-18-9P 380227-19-0P
380227-20-3P 380227-21-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors)

RN 380226-94-8 HCAPLUS
CN Piperidine, 1-(4-amino-1-oxobutyl)-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

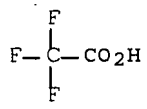
CRN 380226-93-7
CMF C25 H34 N4 O4

Absolute stereochemistry.



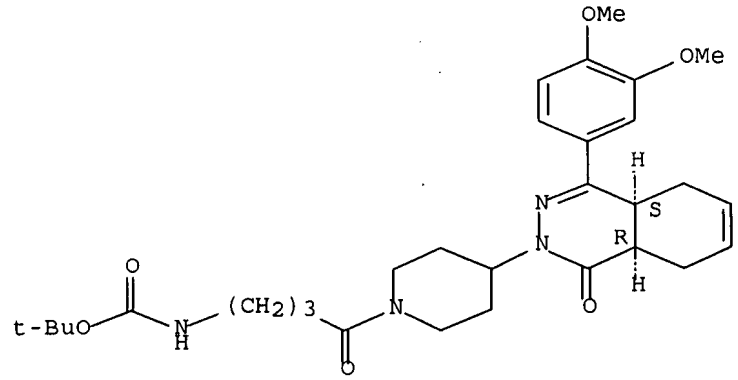
CM 2

CRN 76-05-1
CMF C2 H F3 O2



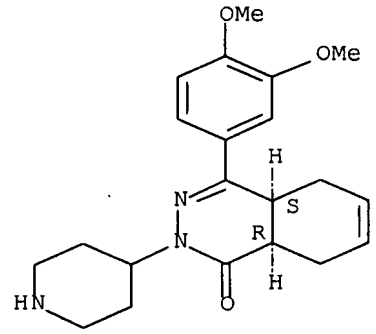
RN 380226-95-9 HCAPLUS
CN Carbamic acid, [4-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-4-oxobutyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



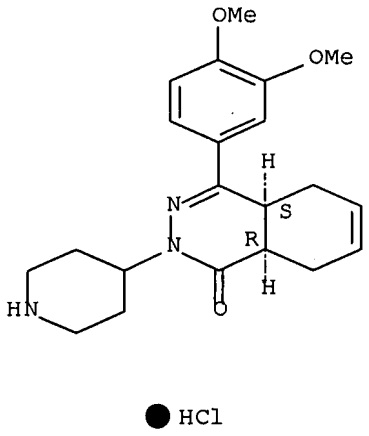
RN 380226-96-0 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



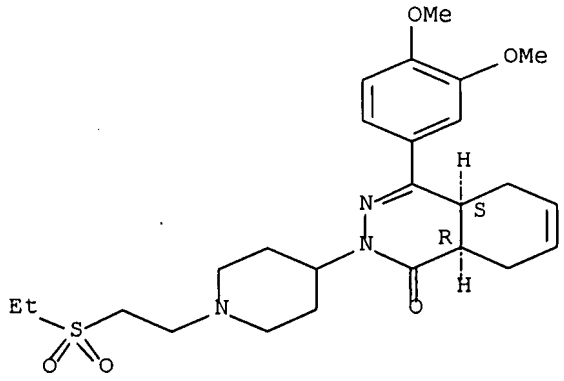
RN 380226-97-1 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380227-08-7 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-2-[1-[2-(ethylsulfonyl)ethyl]-4-piperidinyl]-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

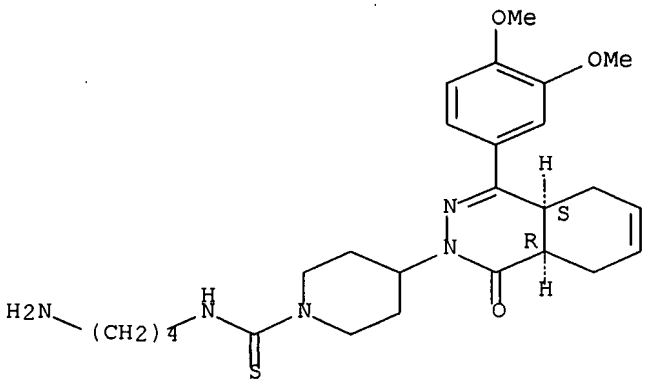


RN 380227-10-1 HCAPLUS
CN 1-Piperidinecarbothioamide, N-(4-aminobutyl)-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

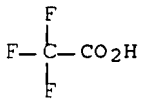
CRN 380227-09-8
CMF C26 H37 N5 O3 S

Absolute stereochemistry.



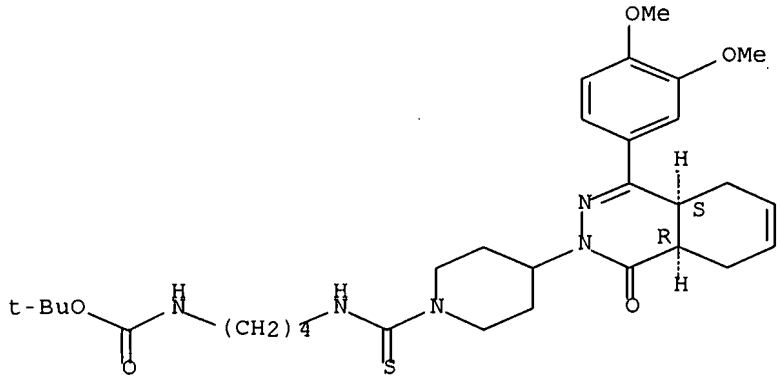
CM 2

CRN 76-05-1
CMF C2 H F3 O2



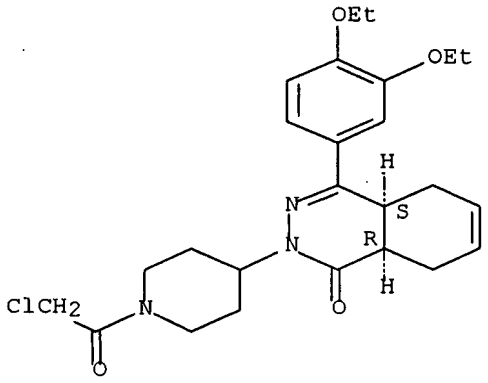
RN 380227-11-2 HCAPLUS
CN Carbamic acid, [4-[[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]thioxomethyl]amino]butyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



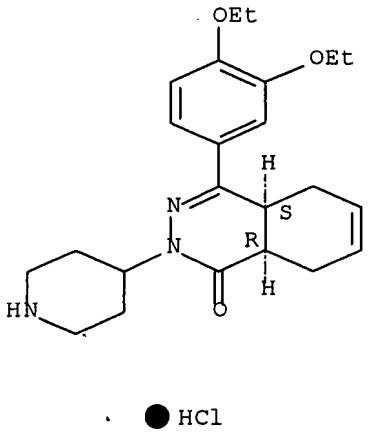
RN 380227-12-3 HCAPLUS
CN Piperidine, 1-(chloroacetyl)-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380227-13-4 HCAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

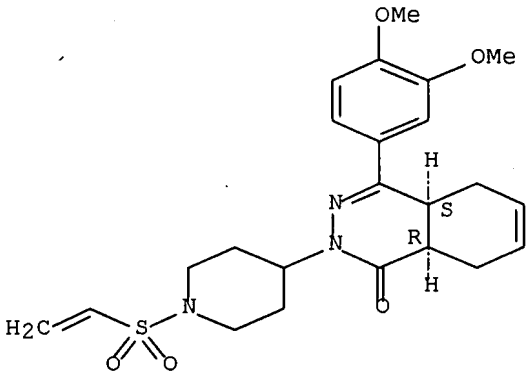
Absolute stereochemistry.



● HCl

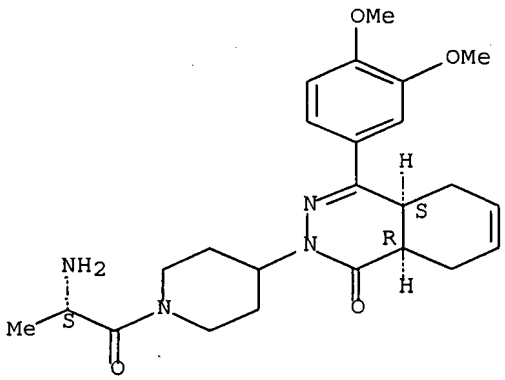
RN 380227-14-5 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(ethenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



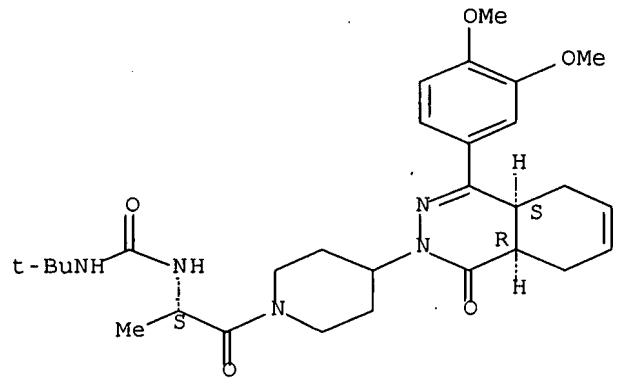
RN 380227-15-6 HCAPLUS
CN Piperidine, 1-[(2S)-2-amino-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



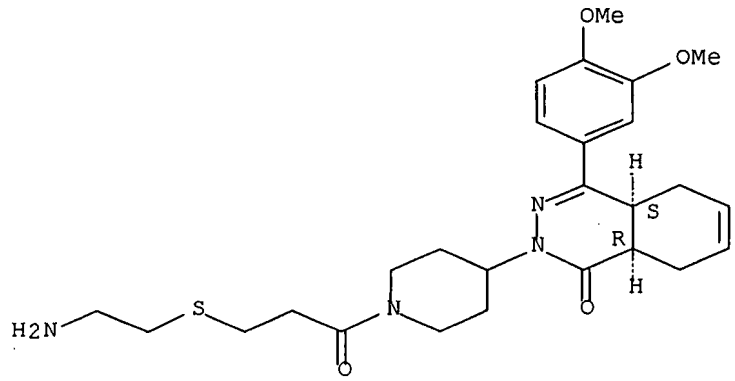
RN 380227-16-7 HCAPLUS
CN Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(2S)-2-[[[(1,1-dimethylethyl)amino]carbonyl]amino]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



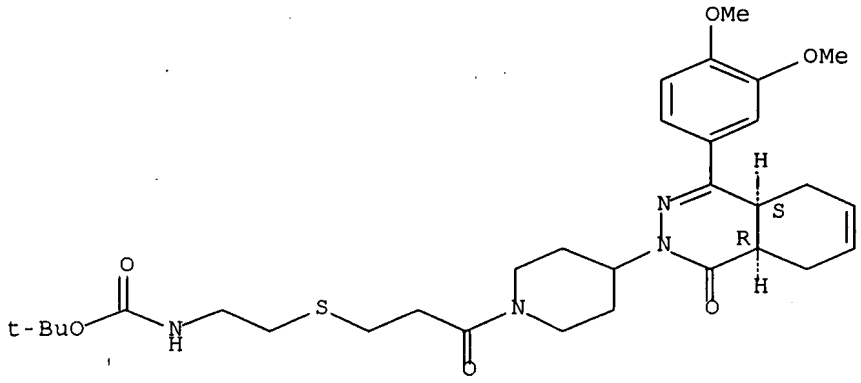
RN 380227-17-8 HCAPLUS
CN Piperidine, 1-[3-[(2-aminoethyl)thio]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380227-18-9 HCAPLUS
CN Carbamic acid, [2-[[3-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-3-oxopropyl]thio]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

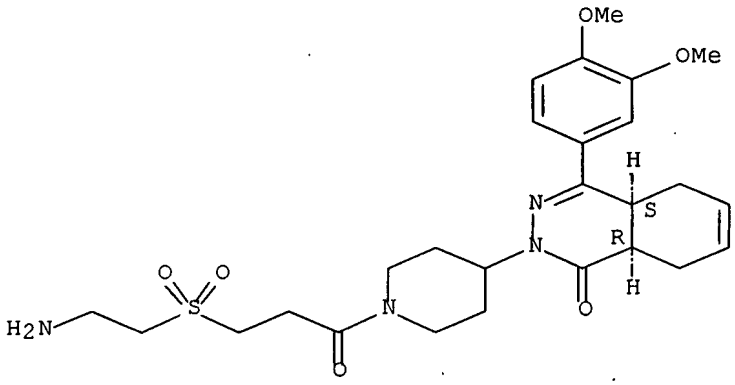
Absolute stereochemistry.



RN 380227-19-0 HCAPLUS
CN Piperidine, 1-[3-[(2-aminoethyl)sulfonyl]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

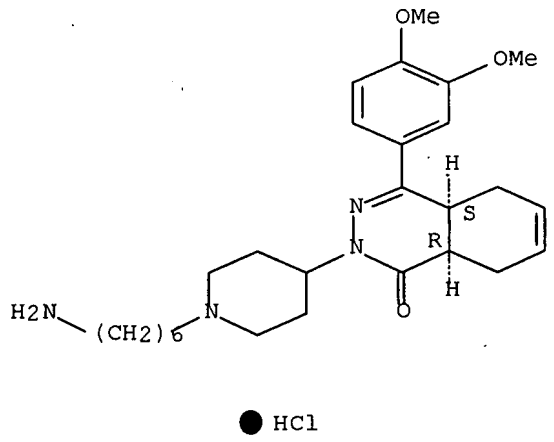


PAGE 2-A

● HCl

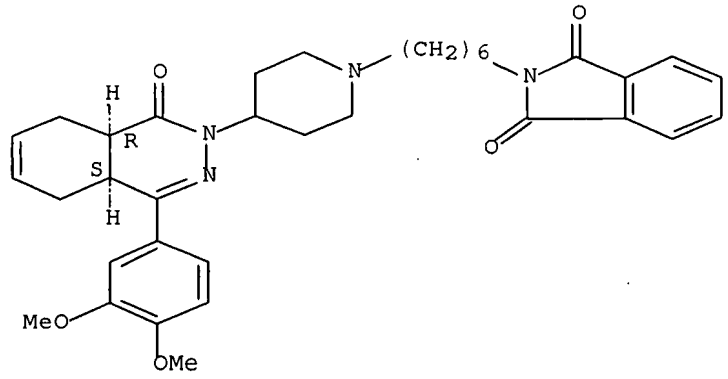
RN 380227-20-3 HCAPLUS
CN 1(2H)-Phthalazinone, 2-[1-(6-aminohexyl)-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, monohydrochloride, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 380227-21-4 HCAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-[6-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]hexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IC ICM C07D237-14
ICS C07D237-22; C07D237-32; C07D405-04; A61K031-50; A61K031-501; A61K031-502; A61P011-06
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): **1**
IT 380226-19-7P 380226-21-1P 380226-23-3P 380226-25-5P 380226-27-7P
380226-29-9P 380226-31-3P 380226-32-4P 380226-34-6P 380226-36-8P
380226-38-0P 380226-40-4P 380226-42-6P 380226-44-8P 380226-46-0P
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380226-56-2P 380226-58-4P 380226-60-8P 380226-62-0P
380226-64-2P 380226-65-3P 380226-67-5P
380226-69-7P 380226-71-1P 380226-72-2P
380226-74-4P 380226-76-6P **380226-77-7P**
380226-78-8P 380226-80-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors)

IT 210466-74-3P 210466-96-9P 210467-52-0P 210467-55-3P 210467-58-6P
227967-30-8P 227967-33-1P 380226-81-3P 380226-82-4P 380226-83-5P
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380227-20-3P 380227-21-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors)

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:659350 HCAPLUS Full-text
DOCUMENT NUMBER: 131:286274
TITLE: Preparation of propanolamine tetrahydro-5H-benzocycloheptene derivatives as β3 adrenergic receptor agonists
INVENTOR(S): Taniguchi, Kiyoshi; Sakurai, Minoru; Fujii, Naoaki; Hosoi, Kumi; Tomishima, Yasuyo; Takasugi, Hisashi; Sogabe, Hajime; Ishikawa, Hirofumi; Hanioka, Naomi
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951564	A1	19991014	WO 1999-JP1500	19990325 <--
W: BR, CA, CN, JP, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1070046	A1	20010124	EP 1999-909333	19990325 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002512639	T	20020423	JP 1999-544560	19990325 <--
EP 1382333	A2	20040121	EP 2003-21612	19990325 <--
EP 1382333	A3	20040204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
US 6495546	B1	20021217	US 2000-646878	20001122 <--
US 2002120148	A1	20020829	US 2002-74020	20020214 <--
US 6635634	B2	20031021		

PRIORITY APPLN. INFO.:		
AU 1998-2826	A	19980406 <--
AU 1998-5058	A	19980804 <--
EP 1999-909333	A3	19990325 <--
WO 1999-JP1500	W	19990325 <--
US 2000-646878	A1	20001122 <--

OTHER SOURCE(S): MARPAT 131:286274

ED Entered STN: 15 Oct 1999

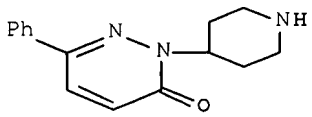
AB Propanolamine tetrahydro-5H-benzocycloheptenes (I) [where R1 = (un)substituted aryl; R2 = H or amino protective group; R3 and R4 = independently H, halogen, OH, NO2, (un)substituted NH2, carboxy, aryl, or alkyl, etc.; R5 = H, alkyl, or aryl; A = (un)substituted lower alkylene; X = O, S, SO, SO2, or NH; m = 0 or 1], and their salts, were prepared as β3 adrenergic receptor agonists. For example, (2S)-3-phenoxy-1,2- epoxypropane was couple with N-benzyl-(3-methoxy-6,7,8,9-tetrahydro-5H- benzocyclohepten-6-yl)amine (preparation given) and treated with Yb(III) trifluoromethanesulfonate to afford (S)-(II). Title compound (S)-(III).HCl reversed carbachol induced increase in intravesical pressure in anesthetized dogs with an ED50 (μg/kg) of 10.8. Three comparison compds. gave similar results. In a test measuring the effect of a comparison compound on cystometrogram, male rats showed an increase in bladder capacity with administration of a 0.01 mg/kg dose. In a third test, a comparison compound decreased the rhythmic contraction of the bladder to 66% of control at a dose of 0.1 mg/kg in rats. Invention compds. are useful for the treatment of pollakiuria or urinary incontinence due to their gut selective sympathomimetic, anti-ulcerous, anti-pancreatitis, lipolytic, anti-urinary incontinence and anti-pollakiuria activities.

IT **246262-38-4**

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of propanolamine tetrahydro-5H-benzocycloheptene derivs. as β3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)

RN 246262-38-4 HCAPLUS

CN 3(2H)-Pyridazinone, 6-phenyl-2-(4-piperidinyl)- (CA INDEX NAME)



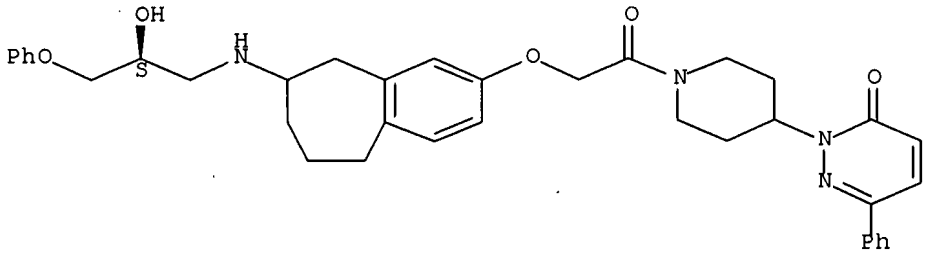
IT **246261-21-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compound; preparation of propanolamine tetrahydro-5H-benzocycloheptene derivs. as β3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)

RN 246261-21-2 HCAPLUS

CN Piperidine, 4-(6-oxo-3-phenyl-1(6H)-pyridazinyl)-1-[[[6,7,8,9-tetrahydro-8-[[(2S)-2-hydroxy-3-phenoxypropyl]amino]-5H-benzocyclohepten-2-yl]oxy]acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

IC ICM C07C217-38
ICS A61K031-135

CC 25-25 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): **1**

IT 61-49-4 75-26-3, Isopropyl bromide 78-96-6 96-41-3, Cyclopentanol 96-50-4, 2-Thiazolamine 99-09-2 99-98-9 100-46-9, Benzylamine, reactions 100-60-7 103-32-2 103-49-1 103-67-3 103-90-2, 4-Acetylaminophenol 104-13-2 104-78-9 104-94-9 105-36-2, Ethyl bromoacetate 106-47-8, reactions 106-49-0, reactions 106-94-5 108-98-5, Thiophenol, reactions 110-68-9, N-Methylbutylamine 111-26-2, n-Hexylamine 156-87-6 371-40-4 372-19-0 455-14-1 496-15-1 501-53-1, Benzyl chloroformate 529-34-0, 1-Tetralone 540-88-5, tert-Butyl acetate 589-08-2 589-09-3, Allylphenylamine 608-43-5, 2,3-Dimethylbenzene-1,4-diol 625-43-4 627-42-9, 2-Chloroethyl methyl ether 753-90-2 768-56-9 826-73-3, 6,7,8,9-Tetrahydrobenzocyclohepten-5-one 841-77-0 994-30-9, Chlorotriethylsilane 1663-39-4 2038-03-1, 4-Morpholineethanamine 3731-51-9, 2-Pyridinemethanamine 3963-62-0 5036-48-6, 1H-Imidazole-1-propanamine 5292-43-3, tert-Butyl bromoacetate 5638-76-6 6291-85-6 6793-92-6, 4-Benzyloxybromobenzene 6829-40-9 7677-24-9, Trimethylsilyl cyanide 7693-46-1, 4-Nitrophenyl chloroformate 13185-18-7, 8-Methoxy-1-tetralone 13214-66-9, Benzenebutanamine 13258-63-4, 4-Pyridineethanamine 13325-10-5 13360-63-9 13952-84-6, 2-Butanamine 16245-79-7 20193-20-8 22236-10-8 35161-70-7 35771-41-6 50541-93-0 60699-67-4, 3-Oxiranylpyridine 62600-71-9, (R)-3-Chlorophenyl oxirane 64208-31-7 70987-78-9 71031-03-3 111622-08-3 113826-06-5 122797-04-0 141498-80-8 152356-05-3 152356-06-4 152356-09-7 152356-10-0 152356-12-2 152356-64-4 213266-45-6 246258-97-9 246262-24-8 246262-25-9 246262-26-0 246262-27-1 246262-29-3 246262-30-6 246262-31-7 246262-32-8 246262-33-9 246262-34-0 246262-35-1 246262-37-3 **246262-38-4** 246262-39-5 246262-40-8 246526-44-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of propanolamine tetrahydro-5H-benzocycloheptene derivs. as β3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)

IT 246259-16-5P 246259-17-6P 246259-18-7P 246259-19-8P 246259-20-1P 246259-21-2P 246259-22-3P 246259-23-4P 246259-24-5P 246259-25-6P 246259-26-7P 246259-27-8P 246259-28-9P 246259-30-3P 246259-32-5P 246259-33-6P 246259-34-7P 246259-35-8P 246259-36-9P 246259-37-0P 246259-38-1P 246259-39-2P 246259-41-6P 246259-42-7P 246259-43-8P 246259-44-9P 246259-46-1P 246259-47-2P 246259-48-3P 246259-49-4P 246259-50-7P 246259-52-9P 246259-53-0P 246259-54-1P 246259-55-2P 246259-56-3P 246259-57-4P 246259-59-6P 246259-60-9P 246259-61-0P 246259-62-1P 246259-63-2P 246259-64-3P 246259-65-4P 246259-66-5P

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246261-55-2P 246261-56-3P 246262-42-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compound; preparation of propanolamine tetrahydro-5H-benzocycloheptene derivs. as β3 adrenergic receptor agonists for treatment of pollakiuria or urinary incontinence)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     FILE 'REGISTRY' ENTERED AT 12:13:29 ON 17 OCT 2007
L3             STRUCTURE UPLOADED
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L4           0 SEA SSS SAM L3

     FILE 'HCAPLUS' ENTERED AT 12:17:05 ON 17 OCT 2007
L5           1 SEA ABB=ON  PLU=ON  US20070179146/PN
               D ALL

     FILE 'REGISTRY' ENTERED AT 12:18:12 ON 17 OCT 2007
L6           1 SEA ABB=ON  PLU=ON  9036-21-9/RN
               D STR
L7           1 SEA ABB=ON  PLU=ON  862578-42-5/RN
               D STR

     FILE 'HCAPLUS' ENTERED AT 12:22:47 ON 17 OCT 2007
               SEL RN L5

     FILE 'REGISTRY' ENTERED AT 12:23:02 ON 17 OCT 2007
L8          47 SEA ABB=ON  PLU=ON  (103008-51-1/BI OR 109-01-3/BI OR 123-56-8/
               BI OR 133-59-5/BI OR 17347-61-4/BI OR 185406-76-2/BI OR
               1899-93-0/BI OR 21615-34-9/BI OR 2840-69-9/BI OR 2859-78-1/BI
               OR 380226-98-2/BI OR 4430-05-1/BI OR 49584-26-1/BI OR 5117-12-4
               /BI OR 56542-67-7/BI OR 69360-26-5/BI OR 85-41-6/BI OR
               862578-18-5/BI OR 862578-19-6/BI OR 862578-20-9/BI OR 862578-21
               -0/BI OR 862578-22-1/BI OR 862578-24-3/BI OR 862578-25-4/BI OR
               862578-26-5/BI OR 862578-27-6/BI OR 862578-28-7/BI OR 862578-29
               -8/BI OR 862578-30-1/BI OR 862578-31-2/BI OR 862578-32-3/BI OR
               862578-33-4/BI OR 862578-34-5/BI OR 862578-35-6/BI OR 862578-36
               -7/BI OR 862578-37-8/BI OR 862578-38-9/BI OR 862578-39-0/BI OR
               862578-42-5/BI OR 862578-44-7/BI OR 862578-46-9/BI OR 862578-48
               -1/BI OR 862578-51-6/BI OR 862578-54-9/BI OR 9036-21-9/BI OR
               98-59-9/BI OR 98-88-4/BI)
L9             STRUCTURE UPLOADED
               D
L10         13 SEA SSS SAM L9
L11         13 SEA SSS SAM L9
L12        258 SEA SSS FUL L9
L13         24 SEA ABB=ON  PLU=ON  L12 AND L8

     FILE 'HCAPLUS' ENTERED AT 13:25:31 ON 17 OCT 2007
L14         27 SEA ABB=ON  PLU=ON  L12
L15         26 SEA ABB=ON  PLU=ON  L14 NOT L5
L16         25 SEA ABB=ON  PLU=ON  L15 AND (AY<2005 OR PY<2005 OR PRY<2005)
               D SCAN L5
L17            QUE ABB=ON  PLU=ON  PHARMAC?/SC,SX
L18         18 SEA ABB=ON  PLU=ON  L16 AND L17
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                SAVE TEMP L18 JAI836HCAP/A

     FILE 'REGISTRY' ENTERED AT 13:33:17 ON 17 OCT 2007
                SAVE TEMP L12 JAI836REGL1/A

     FILE 'HCAPLUS' ENTERED AT 13:34:15 ON 17 OCT 2007

L19           79 SEA ABB=ON  PLU=ON  MENGE W?/AU
L20           88 SEA ABB=ON  PLU=ON  STERK G?/AU
L21            9 SEA ABB=ON  PLU=ON  L19 AND L20
L22          158 SEA ABB=ON  PLU=ON  L19 OR L20
L23           11 SEA ABB=ON  PLU=ON  L22 AND L14
L24           13 SEA ABB=ON  PLU=ON  L21 OR L23
                D AU TI 1-6
                SAVE TEMP L24 JAI836HCAIN/A

     FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:40:58 ON 17 OCT 2007
L25            0 SEA ABB=ON  PLU=ON  L12 AND (MEDLINE/LC OR BIOSIS/LC OR
                DRUGU/LC OR EMBASE/LC)

     FILE 'REGISTRY' ENTERED AT 13:42:26 ON 17 OCT 2007
L26            0 SEA ABB=ON  PLU=ON  L12 AND (MEDLINE/LC OR BIOSIS/LC OR
                DRUGU/LC OR EMBASE/LC)

     FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:43:19 ON 17 OCT 2007
L27            0 SEA ABB=ON  PLU=ON  L21
L28          348 SEA ABB=ON  PLU=ON  L22
L29           26 SEA ABB=ON  PLU=ON  L28 AND (PDE4(W) INHIBIT? OR PYRIDAZIN?)
L30           38 SEA ABB=ON  PLU=ON  L28 AND PIPERIDIN?
L31            9 SEA ABB=ON  PLU=ON  PHOSPHODIESTERASE(W) 4 AND L28
L32           27 SEA ABB=ON  PLU=ON  L29 OR L31
L33      1453591 SEA ABB=ON  PLU=ON  RESPIRATOR?
L34            0 SEA ABB=ON  PLU=ON  L32 AND L33

     FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE, HCAPLUS' ENTERED AT 13:47:09 ON 17
     OCT 2007
L35           26 DUP REM L32 L24 (14 DUPLICATES REMOVED)
                     ANSWERS '1-5' FROM FILE MEDLINE
                     ANSWERS '6-12' FROM FILE BIOSIS
                     ANSWER '13' FROM FILE DRUGU
                     ANSWERS '14-26' FROM FILE HCAPLUS
L36           26 SEA ABB=ON  PLU=ON  L32 AND PHTHALAZINONE?
                SAVE TEMP L36 JAI836MULTIN/A
L37           23 SEA ABB=ON  PLU=ON  L36 NOT L18
                SAVE TEMP L37 JAI836MULTIN/A

     FILE 'STNGUIDE' ENTERED AT 13:50:39 ON 17 OCT 2007
                D COST
                D QUE L24
                D QUE L37

     FILE 'HCAPLUS, MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 13:51:40 ON 17
     OCT 2007
L38           24 DUP REM L24 L37 (12 DUPLICATES REMOVED)
                     ANSWERS '1-20' FROM FILE HCAPLUS
                     ANSWER '21' FROM FILE MEDLINE
                     ANSWERS '22-24' FROM FILE BIOSIS
                D L38 1-24 IBIB AB
                D QUE L18
                D QUE L26
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D L18 IBIB ED AB HITSTR HITIND 1-18